FETAL CELL TECHNOLOGIES INTERNATIONAL, INC.

THE WORLD'S ONLY PROVIDER OF FETAL PRECURSOR STEM CELL TRANSPLANTS

20 YEARS IN RESEARCH & DEVELOPMENT

10 YEARS AHEAD IN BIO TECHNOLOGY & KNOW HOW

10 YEARS OF STEM CELL PRODUCTION

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Fetal Precursor Stem Cell Therapy
TO AVOID INTERRUPTIONS, PLEASE SWITCH OFF YOUR CELLPHONES. THANK YOU.
Educational Seminar

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The Manufacturing Facilities in Europe

7 ha. built up plant area, 15 ha. Land area.

Located in the industrial zone of the city of Nitra (1.5hr from Vienna International Airport) Slovakia, a member of the European Union (EU) since 2003 and current Europe’s fastest growing economy.
GMP Standards in accordance with the European Union (EU) Regulations
Stem Cell Therapy is:

- an implantation of live tissue fragments of different organs and tissues
- of human (allo-) or animal (xeno-) origin,
- from fetal, neonatal, juvenile, or adult stage,
- for the treatment of diseases of humans and animals
Stem Cell Therapy is:

- The only known therapy to help repair or heal any mal/non-functioning cell type of any tissue(s) and organ(s) damaged by disease, injury or by abnormal growth & development

- *Either by direct stimulation of regeneration* of the patient’s own mal/non-functioning cells of any such damaged tissue(s) or organ(s)

or

- *By therapy of new Stem Cells in the patient’s body* to replace the function of damaged or destroyed cells
Stem Cell Therapy can be:

- Implantation by an injection route (or via minor surgery)
- Implantation via major operation
- Surface application of cell transplants
Implantation by an injection route (or via minor surgery):

- intra-muscular
- subaponeurotic (of m. rectus abdominis)
- intrathecal via lumbar puncture
- deep subcutaneous (epifascal)
- intra-hepatic
- intra-venous (intraportal, via portal vein)
- intra-omental (via laparoscopy)
- intra-peritoneal
- intra-arterial (directly or via catheter)
- intra-splenic
- intra-thymic
- intra-cerebral or intra-ventricular (via stereotactic neurosurgery)
- intra-articular
- intra-osseous
Implantation by a major surgery:

- Orthopedic surgery
- Neurosurgery
- Reconstructive surgery

Surface application of Stem Cell Therapy for:

- treatment of deep burns requiring skin grafting
- treatment of ageing surface tissues of the body
The liver is immunoprotective, so it does not reject any foreign cells. No one has yet been able to determine why.

- Direct intra-hepatic implantation is fraught with complications.

- Intra-portal implantation is much safer, particularly if the umbilical vein can be re-opened. However, repeated intra-portal implantation is very dangerous due to risk of intra-portal coagulation.

- Implantation of stem cell therapy into sub-aponeurotic space of muscle rectus abdominis serves same purpose as direct intra-hepatic implantation, but the procedure is simpler and safer, and it can be repeated as many times as necessary.
The **anatomical space** under aponeurosis of m. rectus abdominis, particularly above umbilicus, contains many **anastomotic channels** between systems of v. portae and v. cavae inferioris,

**specifically between accessory portal system of Sappey,**

consisting of tributaries of v.portae at the site of obliterated fetal circulation: vv. para-umbilicales in the ligamentum falciformis and ligamentum teres) **v. epigastricae and v. mammaris interna** (caput medusae) and

**diaphragmatic branches of v. azygos** of systemic circulation

as well as between peri-portal lymphatic channels and tributaries of ductus lymphaticus.

- **Lymphatic vessels** from the upper and anterior surface of the liver pass into falciform ligament, turn upward along superior epigastric vessels to join lower para-sternal lymph-nodes.

- **Lymphatic channels** along superior epigastric vessels cross abundantly area of stem cell transplants if implanted according to FCTI method.
Entire modern science of cell biology is based on premise that all eukaryotic cells are constructed, and carry out their function, in accordance with the same laws:

1. Organ Specificity
2. Homing Principle
3. Principle of Homology
4. Similarity in Genetics
5. Life cycle of cells
Main cells of the same organ are the same, (or almost the same) regardless of the species of origin.

i.e. corresponding cells of identical organs (or tissues) of various animal species (including man) are biologically similar.

There are no antigenic differences between the corresponding cells of organs and tissues of humans and animals of different taxonomic groups – this is another proof of ‘organospecificity’.
Implanted clusters of particular ('prescribed') cells of a specific organ or tissue of a donor (i.e. stem cell transplants) disappear from the host implantation site, usually within 48 hours,

and

75% of implanted stem cells incorporate within 5 to 7 days into the identical organ & tissue of the host they originate from.

If stem cell therapy implanted into a patient is the same as that of diseased organ or tissue, then transplanted cells incorporate into the diseased organ or tissue, with therapeutic effect.

If stem cell transplant implanted into a patient is the same as that of normal ('non-diseased') organ or tissue, then transplanted cells disperse throughout the organism of a patient, without any therapeutic effect. *(Halsted principle, 1909)*
All biological systems not only employ similar principles of cell structure and organization, they are also composed of the same types of chemical molecules.

- Proteins from various organisms of different species are homologous of each other: it means their similarity is significant over the entire amino acid sequence.
- Homologous proteins carry out similar functions.

**Similarity of the amino acid sequence is an indication that homologous proteins evolved from a common ancestor, and thus belong to the same ‘family’**.
4. Similarity in Genetics

- Central dogma of molecular biology:

  DNA directs synthesis of RNA, and in turn RNA directs the assembly of all proteins’ applies to all known living organisms.

- Genetic encoding is universal, the same for all known organisms, which implies that life on Earth has evolved only once.

  ‘Families of similar genes encode proteins with similar or related functions.’
A cell in an organism is not a steady-state system: the course of its life, the “cell cycle”, is dynamic, controlled by an internal clock.

Cell replication, encoded by DNA and executed by proteins,

- sets off a process of cell growth,
- whereby DNA is duplicated and proteins are made,
- followed by a cell division, when two daughter cells arise,
- replacing worn out cells, or
- adding to the cell count, depending what the body needs.
Unique Properties of Fetal Cells (1)

1) High level of readiness to differentiate and to undergo changes
   - in response to environmental stimuli
   - in accordance with own genetic make-up

2) Easy adaptability, due to the plasticity of tissues, which
   - gradually decreases with each successive fetal stage, and
   - disappears at the end of development,
   included are: growth, migration, mobility, ability to create cell-to-cell contacts

3) Highest frequency and speed of cell division, and proliferation, which diminish with advancing development
4) Highest production of various biological substances e.g. growth factors, etc., which facilitate survival of cells after implantation and stimulate damaged tissues and organs of the host

5) Lower immunogenicity with consequently much weaker immune response of the host, as compared with implantation of cells of adult origin

6) Capability of survival on lesser amount of oxygen and on energy supplied by glycolysis alone

which is important during preparation of Fetal Precursor Stem Cell Therapy and for the first few hours after implantation
Vitally important for success is:

METHOD OF PREPARATION OF TISSUE FRAGMENTS FOR FETAL PRECURSOR STEM CELL THERAPY

PREFERABLY BY PRIMARY TISSUE CULTURE

EQUALLY APPLICABLE TO STEM CELL ALLO- OR XENO- TRANSPLANTATION
FCTI Patented Method of Primary Tissue Culture

Creation of ideal growth conditions for one cell type of a tissue or an organ,

- necessary for treatment effect,
- unfavorable at the same time for all other cell types of the same tissue or organ, which are useless for therapeutic effect and which creates an ‘antigenic overload’ as well, that triggers immune reactions (which otherwise would not occur.)
FCTI’s Fetal Precursor Stem Cell Therapy Manufacturing Method

1. assures non-immunogenicity of cell transplants, so that immunosuppression is not required, and

2. by incorporating the pertinent requirements of

PHS Guidelines on Infectious Disease Issues in Xenotransplantation” of January 19, 2001 (Federal Register, Volume 66, Number 19, pages 8120-1)

also

assures to the greatest degree offered by modern science a lack of transmission of diseases by fetal precursor stem cell therapy to the recipient / patient, i.e. between species.
“Because transplantation bypasses most of the patient’s usual protective physical and immunological barriers, transmission of known and/or unknown infections to humans through xeno-transplants may be facilitated.” (61FR49920)

This concern has led FCTI to select rabbits as animal source of its fetal precursor stem cell therapy:

1. **The natural barrier** has been known to prevent transmission of infections between species to a substantial degree.

2. **The more distant the species are**, the stronger has been this natural barrier. It has been 100% true between rabbit and man. To-date there have been no reports of rabbit-to-man transmission of any virus.

3. **No retrovirus** has been found in rabbits to-date!

4. Coming from a **healthy closed colony**, the fetal and newborn rabbits have been found remarkably free of any disease.
ANOTHER REASON for making rabbits a source of FCTI Fetal Precursor Stem Cell Therapy is that rabbit insulin differs from human only by two amino acids, and is therapeutically as effective as porcine, widely used in human medicine.

Rabbits are an excellent source of fetal precursor stem cell therapy because:

A. It is a common knowledge that none of the known viral diseases of rabbits are transmissible to man.

B. There is no argument about the existence of retroviruses in other animal species, but no one has been able to find any retroviruses in rabbits as yet.
FCTI’s Method of Handling Transmission of Zoonoses (3)

According to the following publications:


No viruses of the Genus Retroviridae have been classified or taxonomically recognized in rabbits to-date.
Even if rabbit retro-viruses would be found in the future, they would hardly be infectious to man or other animals.

Not even under extreme experimental conditions could hares be infected by the virus of hemorrhagic pneumonia of rabbits, and likewise the virus of hemorrhagic pneumonia of hares could not be transmitted to rabbits, so it is not surprising that man or other animals could not be infected either.

**NOTE**: There are no reports of prions in rabbits. Since no one has come up with an idea to feed rabbits with animal protein, it is doubtful that any prions will ever be found in rabbits.

C. It is a proven scientific fact that fetal precursor stem cell therapy between discordant species cause much less severe immunological reactions than fetal precursor stem cell therapy between concordant species. Rabbits are phylogenetically distant from man, e.g. ‘discordant’.
Comparative Microphotographs of stem cell transplants (Islets of Pancreas) from rabbit and human

- Animal Adult
- Human Adult
- Animal Fetus
- Human Fetus
- Native Fetal Cell Xenotransplantation
- Stained Fetal Cell Xenotransplantation
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Comparative Microphotographs of stem cell transplants (Hepar) from rabbit and human

Animal Adult

Human Adult

Animal Fetus

Human Fetus

Native Fetal Cell Xenotransplantation

Stained Fetal Cell Xenotransplantation
In 1984 the USSR Ministry of Health Regulations stated that immunosuppression is not necessary for cell transplantation if stem cell (allo- or xeno-) transplants are prepared by primary tissue culture.

Numerous clinical studies proved that no significant clinical or laboratory changes indicative of immunological reactions are observed after stem cell (allo- or xeno-) transplantation.
Indication of Fetal Precursor Stem Cell Therapy (FPSCT)
1. Diabetes mellitus types 1 and mixed 1/2, particularly when complications have already developed, such as:
   a. Diabetic Retinopathy
   b. Diabetic Nephropathy
   c. Diabetic Polyneuropathy
   d. Diabetic Lower Extremity Arterial Disease as well as
      - Brittle Diabetes Mellitus in children and
      - Diabetes Mellitus in pregnancy, or diabetes mellitus as a
        cause of female infertility and habitual pregnancy loss

2. Other hormone deficiency disorders where hormone replacement therapy could not re-establish a normal hormonal balance

3. Early menopause and some other serious gynecological diseases, where state-of-art treatment has failed
Indications (2)

4. Male and female infertility where usual treatment has failed

5. Immune deficiency disorders such as chronic weakness syndrome, AIDS, cancer, etc., as well as autoimmune illnesses

6. Ageing disease including menopause, impotence, depression

7. Parkinson’s and other degenerative diseases of CNS

8. Degenerative diseases of cardiovascular system, liver, gastrointestinal tract, and other organ systems

9. Genetic and chromosomal diseases of children, such as Down syndrome, as well as failure to thrive, mental retardation, frequent illnesses, etc., due to various prenatal, natal and postnatal causes;

10. Others: burns, reconstructive surgery
Contraindications

Absolute:
- terminal stages of disease(s)
- severe acute exhaustion

Temporary:
- acute infection
- untreated chronic infection
- uncontrollable severe hypertension
- uncontrollable severe allergic status
Treatment of complications of type 1 diabetes mellitus (IDDM) by Fetal Precursor Stem Cell Therapy (FPSCT)
Fetal Precursor Stem Cell Therapy VS treatment by individual hormones

• hormones are produced, and released, by organism as necessary, there is no storage of active hormones;

• hormones have only short-term effect, while FPSCT has long-term therapeutic benefit;

• hormone replacement therapy is a treatment for life, without possibility of cure;

• long-term hormone replacement therapy will suppress the respective endocrine gland, and cause atrophy and loss of function of the gland.
Insulinotherapy VS Fetal Precursor Stem Cell Therapy

- insulin cannot cure diabetes mellitus;

- insulin cannot prevent disabling - often life threatening - complications of diabetes mellitus;

- even the optimal insulinotherapy cannot stop relentless progress of diabetic complications, only FPSCT can.

- But FPSCT cannot replace insulin yet as a life saving treatment! FPSCT must be used simultaneously with insulinotherapy.
Fetal Precursor Stem Cell Therapy can successfully treat complications of diabetes mellitus

In 1978 the first type 1 (IDDM) diabetic patient with retinopathy and nephropathy was successfully treated in Moscow by Cell Transplants – she remained insulin-independent for over 20 years.

Success rate of treatment by FPSCT of

- pre-proliferative stage of diabetic retinopathy: 60% - 70%
- pre-azotemic stage of diabetic nephropathy: 60%
- any stage of diabetic poly-neuropathy: 95%
- pre-obstructive stage of diabetic vasculopathy: 70%
- clinically un-controllable children’s ‘brittle diabetes’ 90%
• 105 patients with complications of diabetes mellitus type 1 received 115 FPSCT of rabbit origin, 27 of them more than once.
• 73 patients in 1st group had subaponeurotic,
• 33 patients in 2nd group had intraportal FPSCT.
• 1st group: 18 – 57 years, median 35.4 years, duration
• 6 – 35 years, median 17.4 years, labile course in 77%, ketoacidosis in 70%, insulin dosage 18 – 96 U.
• 2nd group: 7 – 55 years, median 32.6 years, duration 7 – 25 years, labile course in 88%, ketoacidosis
• in 82%, insulin dosage 18 – 60 U.
## Frequency of IDDM complications, N = 106

<table>
<thead>
<tr>
<th>IDDM Complication</th>
<th>Group # 1</th>
<th>Group # 2</th>
<th>Intraportal FPSCT %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># patients with</td>
<td>I.M. FPSCT%</td>
<td># patients with</td>
</tr>
<tr>
<td>Poly-neuropathy</td>
<td>68</td>
<td>93.1</td>
<td>31</td>
</tr>
<tr>
<td>Peripheral vasculopathy</td>
<td>68</td>
<td>93.1</td>
<td>31</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>57</td>
<td>78</td>
<td>28</td>
</tr>
<tr>
<td>of which proliferative</td>
<td>22</td>
<td>30.1</td>
<td>12</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>50</td>
<td>68.5</td>
<td>19</td>
</tr>
</tbody>
</table>

* FPSCT = Fetal Precursor Stem Cell Therapy
Median Glycaemia (mmol/L)

* P<0.05 in comparison with initial value
** P<0.05 in comparison with the Group 1

<table>
<thead>
<tr>
<th>Implant Site</th>
<th>Pre-FPSCT</th>
<th>14 days post-SCT</th>
<th>1 month post-FPSCT</th>
<th>3 months post-FPSCT</th>
<th>6 months post-FPSCT</th>
<th>1 year post-FPSCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 IM FPSCT</td>
<td>11.7</td>
<td>10.8</td>
<td>8.5</td>
<td>8.7</td>
<td>9.1</td>
<td>10.9</td>
</tr>
<tr>
<td>variance</td>
<td>+/-1.4</td>
<td>+/-1</td>
<td>+/-0.9*</td>
<td>+/-0.9*</td>
<td>+/-1.1*</td>
<td>+/-1</td>
</tr>
<tr>
<td>Group 2 Intra-Portal FPSCT</td>
<td>11.6</td>
<td>10.1</td>
<td>8.9</td>
<td>8.1</td>
<td>8</td>
<td>9.2</td>
</tr>
<tr>
<td>variance</td>
<td>+/-1</td>
<td>+/-0.9</td>
<td>+/-0.8*</td>
<td>+/-0.2*</td>
<td>+/-0.3**</td>
<td>+/-0.6**</td>
</tr>
</tbody>
</table>

* FPSCT = Fetal Precursor Stem Cell Therapy
Changes of HbA1c
* P<0.05 in comparison with initial value
** P<0.05 in comparison with Group # 1

<table>
<thead>
<tr>
<th>Implant Site</th>
<th>Pre-FPSCT</th>
<th>3 months post-FPSCT</th>
<th>6 month post-FPSCT</th>
<th>12 months post-FPSCT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group #1 IM FPSCT</strong></td>
<td>13.8%</td>
<td>9.2%</td>
<td>9.5%</td>
<td>10.2%</td>
</tr>
<tr>
<td>variance</td>
<td>+/-1</td>
<td>+/-0.6*</td>
<td>+/-0.1*</td>
<td>+/-0.4*</td>
</tr>
<tr>
<td><strong>Group #2 Intraportal</strong></td>
<td>12.9%</td>
<td>8.3%</td>
<td>8.4%</td>
<td>8.7%</td>
</tr>
<tr>
<td>FPSCT</td>
<td>+/-1.5</td>
<td>+/-0.2*</td>
<td>+/-0.3*</td>
<td>+/-0.9**</td>
</tr>
</tbody>
</table>

* FPSCT = Fetal Precursor Stem Cell Therapy
## Changes of exogenous insulin dosage (in %)

* P<0.05 in comparison with initial value

** P<0.05 in comparison with Group # 1

<table>
<thead>
<tr>
<th>Implant Site</th>
<th>Pre-FPSCT</th>
<th>14 days post-FPSCT</th>
<th>1 month post-FPSCT</th>
<th>3 months post-FPSCT</th>
<th>6 months post-FPSCT</th>
<th>1 year post-FPSCT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IM FPSCT</td>
<td>51.3 IU</td>
<td>49.9 IU</td>
<td>41.2 IU</td>
<td>40.1 IU</td>
<td>41.8 IU</td>
<td>47.4 IU</td>
</tr>
<tr>
<td>% initial</td>
<td>100</td>
<td>89.5</td>
<td>80.3</td>
<td>78.1</td>
<td>81.5</td>
<td>92.4</td>
</tr>
<tr>
<td><strong>Group 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraportal FPSCT</td>
<td>49.3 IU</td>
<td>40.3 IU</td>
<td>33 IU</td>
<td>26.3 IU</td>
<td>25.7 IU</td>
<td>37.1 IU</td>
</tr>
<tr>
<td>% initial</td>
<td>100</td>
<td>81.7</td>
<td>66.9</td>
<td>53.3</td>
<td>52.1</td>
<td>75.2</td>
</tr>
</tbody>
</table>

* FPSCT = Fetal Precursor Stem Cell Therapy
Changes of C-peptide concentration (pmol/l)

* Pk<0.01 in comparison with control group: healthy donors N=20
** P<0.05 in comparison with initial value
^ P<0.05 in comparison with Group # 1

<table>
<thead>
<tr>
<th>Implant site</th>
<th>Cpeptide +/-</th>
<th>Pre-FPSCT</th>
<th>14 days</th>
<th>1 month</th>
<th>3-6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td></td>
<td>0.266 +/- 0.07</td>
<td>post-SCT</td>
<td>post-SCT</td>
<td>post-SCT</td>
</tr>
<tr>
<td>Group #1</td>
<td>Cpeptide+</td>
<td>0.108</td>
<td>0.163</td>
<td>0.166</td>
<td>0.152</td>
</tr>
<tr>
<td>I.M. FPSCT</td>
<td>N=27</td>
<td>+/-0.08*</td>
<td>+/-0.03**</td>
<td>+/-0.05**</td>
<td>+/-0.03**</td>
</tr>
<tr>
<td>Group #2</td>
<td>Cpeptide-</td>
<td>0</td>
<td>0.111</td>
<td>0.173</td>
<td>0.158</td>
</tr>
<tr>
<td>Intraportal</td>
<td>N=18</td>
<td>+/-0.03</td>
<td>+/-0.02</td>
<td>+/-0.04</td>
<td></td>
</tr>
<tr>
<td>FPSCT</td>
<td>Cpeptide+</td>
<td>0.115</td>
<td>0.281</td>
<td>0.18</td>
<td>0.188</td>
</tr>
<tr>
<td></td>
<td>N=15</td>
<td>+/-0.06*</td>
<td>+/-0.09**^</td>
<td>+/-0.04**</td>
<td>+/-0.07**</td>
</tr>
</tbody>
</table>

* FPSCT = Fetal Precursor Stem Cell Therapy
Hormone concentrations post-intraportal FPSCT

* P<0.05 in comparison with starting level
^ P<0.05 in comparison with portal vein level

<table>
<thead>
<tr>
<th>TIME</th>
<th>Portal vein</th>
<th>Hepatic vein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Insulin</td>
<td>Cpeptide</td>
</tr>
<tr>
<td>Initial</td>
<td>4.9</td>
<td>0.12</td>
</tr>
<tr>
<td>1 minute</td>
<td>4.2</td>
<td>0.13</td>
</tr>
<tr>
<td>5 minute</td>
<td>4.2</td>
<td>0.12</td>
</tr>
<tr>
<td>15 min.</td>
<td>4.6</td>
<td>0.11</td>
</tr>
<tr>
<td>30 min.</td>
<td>2.6</td>
<td>0.1</td>
</tr>
<tr>
<td>60 min.</td>
<td>3.5*</td>
<td>0.11</td>
</tr>
</tbody>
</table>

* FPSCT = Fetal Precursor Stem Cell Therapy
Pain syndrome of diabetic distal polyneuropathy

1st group: At 3 months follow-up on 81.4% of patients, the pain disappeared or substantially decreased. After 6 months, the same effect is present in 74.2%, and after 12 months in 50% of patients.

2nd group: At 3 months follow-up, 87.8% of patients were pain-free, and after 12 months, the same effect present in 76.1% patients.
Diabetic lower extremity arterial disease (LEAD)

As compared with normal controls, in diabetic patients:
1/ half-time of Tc99M disappearance from tissue depot was 1.5 times higher,
2/ tissue circulation at rest was substantially lower,
3/ tissue circulation with exercise leading to ischaemia was 3 times lower. - All of above were significant at p<0.01.

After FPSCT:
1/ half-time of Tc99M disappearance from tissue depot decreased,
2/ tissue circulation increased, particularly with exercise leading to ischaemia, both statistically significant at p<0.05.
Repeated FPSCT’s

27 patients had repeated FPSCT, 19 of them I.M., 3 1\textsuperscript{st} intraportal and 5 2\textsuperscript{nd} intraportal FPSCT. Repeated I.M. FPSCT’s are advisable/mandatory as they prolong compensation of diabetes: must be done prior to the further progression of disease.

In 18 patients the previous cell transplantation was allo-transplantation (of human fetal cells). The clinical results of cell allo- and xeno-transplantation in these 18 patients were the same, with the exception of the lowered dose of exogenous insulin: this was 18 – 22 % after xeno-,

and 20 – 60% after allo-transplantation.
Immunological reactions (1)

Cellular immunity: **T lymphocyte count** decreased on 1\textsuperscript{st} day post-fpsct to the level of healthy controls, then on 14 – 20\textsuperscript{th} day, it returned to the initial level (as compared with healthy controls). **Activation index of T lymphocyte** was higher than in healthy controls initially & as well as during the entire follow-up after FPSCT. There were no differences between 1\textsuperscript{st} and 2\textsuperscript{nd} group.

Humoral immunity: In 1\textsuperscript{st} group **B-lymphocyte count** was lower than in healthy controls during the entire study, while in 2\textsuperscript{nd} group in was (14 – 20 days after FPSCT) twice as high as in controls (p<0,05), and four times higher than before FPSCT (p<0,05).

**Concentration of immunoglobulins G, M, A,** remained the same in both groups for the duration of follow-up after FPSCT, and that was the same as in healthy controls.
Conclusions:

1) There were no obvious changes of the immune status of patients after FPSCT when cell transplants were prepared by a FCTI method of primary tissue culture from fetal/newborn rabbits.

2) There were no obvious changes to the immune status of patients after FPSCT as compared with cell allo-transplantation.

3) No statistically significant differences in cellular immunity were found between I.M. and intra-portal implantation sites after FPSCT.

Follow-up at 3 weeks, 3 months, up to 4 years after SCT: 74% stabilization of LEAD, 18% improvement, 8% worsening. Stabilization of retinopathy in 70% of patients, improvement in 25%, worsening in 5%. In 34% improvement of visual acuity, in 60% stabilization, in 6% worsening.
Other reports


55 IDDM patients with LEAD, retinopathy, nephropathy, 80% with vasomotor abnormality, 100% abnormal capillaroscopy, 30% in 1st and 70% of 2nd stage.

During 1 year follow-up after SCT in 73% stabilization, in 22% improvement, in 5% worsening. Ophthalmologic exam: 43% improvement, 57% stabilization. Visual acuity improved in 20%, the same in 80%. 24-hours proteinuria dropped from 1.8 gm/L to 1.2 gm/L.
Other reports


85 IDDM patients, 41% with retinopathy, 11 in 1st stage, 21 in pre-proliferative stage, 3 in proliferative state. (One stage 2, and all stage 3 patients removed because of worsening of nephropathy.)

Follow-up 3 weeks - 4 years after SCT and AXT. In 58 – 86% gradual improvement over 3 – 9 months.

In 24% patients in stage 1a complete regression of retinopathy.

Intercurrent diseases: worsening 6% of patients over 1 – 2 years.
100 IDDM patients with LEAD, 18 – 60 years of age, 72% abnormal rheovascular studies, 100 % abnormal capillaroscopy, 25 in 1\textsuperscript{st} stage, 75 in 2\textsuperscript{nd} stage.

Follow-up 3 weeks – 3 years post SCT: in 74% gradual stabilization, in 10% improvement, in 3% worsening.
Immunological studies (1)


Morozov Y.I., Kirdei E.G., Kim A.Y.: Vlianie ksenotransplantatsii ostrovkovyh kletok podzheludochnoi zhelezi na immunny status bolnych sacharnym diabetom ("Effect of xenotransplantation of islet cells of pancreas on the immune status of diabetic patients"), Klinicheskaia Medicina, Moscow, 1995; 73, pp. 32-34.


...of Stem Cell Transplantation is hypothetical.

There are a few published but rather exceptional reports of autopsy findings where the implanted xeno-cells were found surviving at the implantation site (brain, under the kidney capsule). There are published data of animal experimentation with histological proof of survival of implanted cells at the implantation site.

Authors of the book on cell transplantation as the treatment of diabetes mellitus feel that the clinical effect is mostly a result of direct stimulation of patient's own cells and tissues under the influence of transplanted cells or tissues, rather than the functioning of transplanted cells themselves.
Cell therapy publications state that all implanted cells disappear very quickly from the implantation site, and the greatest portion of them ends within 2 - 3 days in the organ or tissue "where the respective cell belongs", which should be all organs and tissues of the patient which are damaged as a result of a disease, and which are being treated by the implantation of cells or tissue fragments of each such mal-functioning organ or tissue, following the rules of "organospecificity". This hypothesis is supported now by the recent publications dealing with ‘homing’.

If transplanted cells and tissues exert their effect mostly by direct stimulation of the corresponding malfunctioning organs and tissues of the patients, to which they are ‘homed’, the question is raised what is the basis of such direct stimulation: outright metabolic influence, paracrine regulatory effect, messenger function, etc.
Complications of IDDM: We do not understand the cause of underlying microangiopathic changes. It is not the result of lack of insulin. There is a hypothesis that exogenous insulin is the cause of vascular complications of IDDM. Lately it has been believed that lack of C-peptide is the cause of microcirculatory pathology. We think - together with Alexis Carrell - that the problem of IDDM is not only a lack of insulin (Carrel: “Insulin does not cure a diabetic”), but also lack of some (heretofore unknown) factors produced by various cells of the Langerhans islets, besides beta cells.

The chronic deficiency of these factors places great undue demands on the regulatory system of the metabolism of carbohydrates and lipids, primarily the ‘hypothalamic/pituitary - adrenal axis’, and on the liver as the key organ of metabolism, forcing compensation by these organs, which lead to an overload and exhaustion of these organs. The appearance of complications of IDDM is the signal that the system is starting to break down.
Medical Advancement

Fetal Precursor Stem Cell Therapy for Down Syndrome
Trisomy 21, Down syndrome, the most frequent and best known chromosomal disorder with incidence of 1:700 live births, a disorder of the whole body, phenotypically with abnormalities of physical and mental development with a marked immunodeficiency:

1) Somatic, gross motor, intellectual and mental development, are lagging behind norms, and more so with each month of postnatal growth and development;

2) Nanism, hypothyroidism or adrenal insufficiency, are the result of endocrine abnormalities;

3) Disproportionate growth of face and cranium, not obvious at birth, becomes more noticeable with age as a result of cranial growth delays. Brain growth is slowed down disproportionately as well: occipital and parietal lobes lag behind more than the other parts, but the cerebellum is the most affected.
4) Mongoloid physiognomy becomes more noticeable with age.

5) Delayed development of all mesenchymal structures causes immune system deficiency, and increased incidence of leukemia.

6) There is no direct relationship between the degree of visible chromosomal damage and the delay of intellectual development.

7) Nanism begins in infancy but becomes most pronounced in puberty.

Lifespan is shortened, but in absence of congenital heart defects, and serious immunological deficiencies, Down syndrome patients can live up to 60 years of age. There is no reproductive ability in complete trisomy 21, but patients with mosaic forms of trisomy 21 can be fertile and have normal offsprings.
Therapeutic principles:

1) regulation of endocrine balance, in particular hypothyroidism and lowered function of glucocorticoid portion of adrenal cortex;

2) elimination of ever increasing delay in brain development by frequent FPSCT;

3) correction of immune system deficiency by FPSCT;

4) repair of defects of supportive tissues of the body by FPSCT;

5) total rehabilitation of all body systems, by physiotherapy, active exercise, speech therapy, occupational therapy, and all educational tools available;

6) avoidance of therapeutic nihilism.
Standard medicine: *genetic and chromosomal diseases have no known treatment.* Based on many reports from the university hospitals of Germany, U.S.S.R./Russia, Spain, and U.S.A. prior to 1957, etc. on success of *treatment of many genetic and chromosomal diseases by a complex therapeutic protocol based on stem cell transplantation.*

Down syndrome has been a shining example. Prof. Dr. F. Schmid published data about his personal treatment of over 3,400 children with Down syndrome, whereby 25% of his patients were able to attend regular schools, and 50% regular kindergartens. Published data prove the statistically significant improvement in height, skull circumference, index of brain volume, IQ and mental development, motor development. Among untreated children with Down syndrome 50 – 60% dies during the first 5 years of life due to intercurrent infections and cardiac failure, while the mortality of children treated in accordance with Dr. Schmid’s protocol is the same as in normal children.
Typical features of Down syndrome become less pronounced with each subsequent FPSCT treatment and immune system deficiency is completely corrected. In all such cases FPSCT has been carried out at an early age, or as soon as possible after the diagnosis was established. The earlier in life FPSCT was carried out, the better was the outcome, while beyond certain age any such treatment was of questionable benefit: to start stem cell transplantation for a child with Down syndrome beyond the age of 4 years is of minor to minimal therapeutic benefit.

Own published study of the first 83 patients with Down syndrome in which pediatric psychologist evaluated mental and psychological functions before and after FPSCT showed the following.

The percentage of younger Down syndrome children (up to 3.5 years of age) with mental development index of over 50 points increased from 17% before the first FPSCT, to 58% after the first FPSCT, and to 71% after the second FPSCT.
The IQ in the older children (4 - 9 years of age) moved from 25 to 49 points range to 50 - 69 points range, which was statistically significant difference.

Decreased hyperactivity, improvement of impaired concentration, lessened stereotypia and behavioral inertia, and improved speech expressivity, can already be observed already after the 1st cell transplantation, and the difference was statistically significant.

Volume of auditory/visual memory, productivity of thinking in categories, acoustic gnosis, and optic/spatial gnosis, were improved, but not significantly.

After FPSCT there was an improvement in motor function, particularly in fine coordinated movements, and in self-care habits, which were not psychometrically tested.
Immune system deficiency of Down syndrome can be completely corrected.

In our study of two age-matched groups of patients with Down syndrome, a group of 6 patients was treated every 6 months, which is three altogether by transplantation of human fetal cells of medulla alba of brain, brain cortex, and cerebellum, and the control group of 7 patients received implantation of saline.

After 6 months, just before the 2nd cell transplantation, 3 of 7 children in the control group were dead due to infections. In the treated group all children were well.
The decreases of IgA from 166 to 85, and IgM from 140 to 74, in the control group, were signs of immune system deficiency responsible for the death of 3 out of 7 infants, while the marked increase of IgG from 459 to 872 could have been an expression of recurrent infections.

The transplantation of human fetal cells stimulated the immune system, as the levels of IgA increased from 68 to 83, and of IgM from 101 to 111, and that of IgG decreased from 551 to 463, that accounts for lesser frequency and severity of bacterial infections.

A remarkable improvement of the immune system function in treated patients was a result of one treatment by stem cell transplantation only, and in that treatment only fetal cells of three parts of brain were implanted and no cells of immune system organs.
At the age of 3 years, a disfiguring physiognomy, standing and walking only with support, patient doesn't recognize the parents. At this time, she, after-ripening-treatment of Haubold, begins. Four experts negate the possibility of the treatment. The case goes before the German Federal Social Court.

At 14 years of years, Uta attends the 4th grade of a normal school, reads, writes and counts (with mistakes) up to 100. At 21 years of age Uta works in a hospital as a nursing assistant, rides a bus daily to work in the city, and even has a medical insurance that covers all but the treatment of any disease(s) due to Down syndrome.
Comparison of a physiognomy of a male who began treatment late at the age 9 ½ (Before), and his condition at the age 10 1/2 (After).
Down Syndrome – Before and After Treatment

Physiognomy of Down syndrome child that received treatment from four to ten years of age
Physiognomy of Down syndrome child that received treatment from four to ten years of age
Physiognomy of Down syndrome child treated from late infancy on
Down Syndrome – Before and After Treatment

Physiognomy of Down syndrome child treated since infancy

Before

During

After
Physiognomy of Down syndrome child treated since infancy
Down Syndrome – Before and After Treatment

Physiognomy of Down syndrome child treated since infancy

Before

During

After
Down Syndrome – Before and After Treatment

Physiognomy of Down syndrome child treated since infancy
Down Syndrome – Before and After Treatment

Physiognomies of Down syndrome children, whose treatment began after 2 years of age, now between 5-12 years of age.
Pigmentary type of Down syndrome (Traviata type). Physiognomies at different ages. This type is marked by darker skin pigmentation, dark hair and relatively big, expressive eyes.
Pigmentary type of Down syndrome (Traviata type). Physiognomies at different ages. This type is marked by darker skin pigmentation, dark hair and relatively big, expressive eyes.
Pigmentary type of Down syndrome (Traviata type). Physiognomies at different ages. This type is marked by darker skin pigmentation, dark hair and relatively big, expressive eyes.
Series of photographs of a Down syndrome child from the family album: between 2 and 4 years of age.
Down Syndrome – Before and After Treatment

Alopecia of the reddish-blond type of Down Syndrome:

Before treatment at age 6½

Hair 2½ years after start of treatment

Seven months after the beginning of treatment

2½ years after start of treatment
Photographs of an awkward, hypodynamic type of Down Syndrome during the treatment

**Before**
At 1 1/2 years of age; severe expressive (physiognomic) distortion

**During**
At 2 1/2 years of age controlled expression; macroglossia; delay of static development

**After**
At 10 years of age controlled, clear facial expression; patient can speak fluently, reads books, and writes accurately
Progress of an erethic type of Down’s Syndrome during treatment
(at one year intervals):

The pictures show the transformation from an uncontrolled mimicry, to a glassy stare, to a sociable facial expression.

7 years old  8 years old  9 years old  10 years old
Down Syndrome – Before and After Treatment

Progress of expressive (physiognomic) changes of a Down syndrome child

Before
a) at one year of age

During
b) at two years of age

er

After
c) at four years of age
Highly stigmatized Down syndrome girl from a high Alpine valley who, at 2.5 years of age, was unable to speak; was restless, worrisome, and unmanageable.

After four years of treatment – at 6 1/2 years of age, and after attending a normal kindergarten, the child speaks German and Italian, is enrolled in primary school on a trial basis.

Six months after the beginning of treatment, the child already maintains eye contact and pays attention.
Down Syndrome – Before and After Treatment

Progress of a Down syndrome boy at:

Before
1 1/2 years of age

During
at three years of age

After
at nine years of age
Down syndrome boy with chronic infections

at the beginning of treatment

five months later
Down Syndrome – Before and After Treatment

Down syndrome girl at four months of age

**Before**
highly stigmatized facial expression

**After**
considerable normalization of facial expression after five years of treatment
Down Syndrome – Before and After Treatment

Down syndrome girl at seven months of age before treatment

Before after 4.5 years of treatment
Down Syndrome – Before and After Treatment

Photographs of a Down syndrome boy between two and seven years of age (a-f) from the family album
Characteristic change of appearance, mimicry, and pigmentation, of four Down syndrome children under treatment from age two to eight.
Physiognomy and appearance (phenotype) of Down syndrome children treated from ages five to fourteen.
Down Syndrome

Facial expression and appearance of Down syndrome children under treatment since one year of age
Representative cross-section of the appearance of treated Down syndrome boys from age four to fourteen
Down Syndrome – Boy: Marcus

Marcus as an infant.

Still unable to walk.

Marcus on the potty.

Marcus and his younger sister.

The siblings in a sleeping bag.
Play is hard work for the small boy. Marcus “works” with educational toys (coordinating, assigning).
Down Syndrome – Boy: Marcus

Marcus and his sister on a bicycle tour.

Marcus as amateur swimmer.
Fetal Precursor Stem Cell Therapy for Down Syndrome, Cerebral Palsy and other Neurological diseases

• Fetal Precursor Stem Cell Therapy obtained from rabbits kept in closed colony and propagated by primary tissue culture;

• Cultured Fetal Precursor Stem Cell Therapy administered 3 times per year

• Fetal Precursor Stem Cell Therapy as one component of a comprehensive therapy protocol
Characteristics of Down Syndrome

Characteristics of Down Syndrome

Dermoglyphics
Simian crease (40%), missing distal horizontal crease on the little finger (20%)

Cheilosis:
vertically creased and cracked lips.

Unkempt, wiry hair.
Characteristics of Down Syndrome

- ‘Sandal gap or furrow; extended space between 1st and 2nd toe.
- Anomalies of primary dentition; irregular position and multi-pronged incisor teeth.
- Down syndrome pelvis: iliac wings ("elephant ears"); flattened acetabular roof; inward curvature of the hips (coxa valga)
Characteristics of Down Syndrome

Brachydaktyly, acromicria, clinodactily

Syndactylism between 4th and 5th toe

Physiognomy of an untreated mongoloid infant with characteristic facial features and already visible macroglossia
Untreated hypodynamic type of Down Syndrome

Hypodynamic type of Down Syndrome with microphelia; micrognatia of the upper jaw and protruding tongue
Hypodynamic type of Down Syndrome with mimic stare, and strong pigmentation of facial skin.
Characteristics of Down Syndrome

Phases of mimic distortions of a hyperdynamic mongoloid male without real contact to his surroundings. Three pictures taken within a few seconds.
Characteristics of Down Syndrome

Physiognomy of the hyperdynamic type of Down syndrome.

Cheilosis of the lips with low, radial cracks.

Cheilosis of the lips
Characteristics of Down Syndrome

Dystrophy of the nails; hyperkeratosis of the nail

Hyperkeratosis and acne during puberty

Gaping mouth as a permanent condition due to macroglossia and hypertrophic adenoids.
Chronic rhinitis (most frequent symptom of immune deficiency in small children)

Hypoplasia of penis

Hypoplasia and pronounced raphe of the scrotum
Characteristics of Down Syndrome

Development of tongue in Down Syndrome patients at various ages, and degrees of expression from a simple macroglossia with tongue protruding between lips to a severe case of lingua scrotalis.
Iris spots ("Bushfield spots"): stripe-like illumination of the iris.

Hypertelorism, and strabismus

Characteristics of Down Syndrome
Characteristics of Down Syndrome

Epicanthus and iris spots
Anomalies of teeth in Down Syndrome

Anomalies of dentition

Characteristics of Down Syndrome
Characteristics of Down Syndrome

- Multi-pronged incisor teeth
- Oligodontia; pivot teeth
- Pivot- and trapeze-shaped teeth; cheilosis
- Wide spaces between pivot-shaped teeth
Characteristics of Down Syndrome

- Simian crease
- A typical convolution of skin on the knee
- Typical creases in the buttock area
- on sole of the foot
- ‘Sandal Gap’
Characteristics of Down Syndrome

- Fat neck
- Pectus excavatum
- Bull neck
- Abnormally short digits (brachydactyly) and web formation
- Hypertrichosis
- Triangular fleshy mass of thickened connective tissue (pterygium)
Characteristics of Down Syndrome

Various, often extreme, hair abnormalities

Coarse, thick, and wiry hair

Limp, thin, and sparse, hair typical of the diencephalon type of Down Syndrome
Characteristics of Down Syndrome

- Pronounced capillaries with scars after skin ulcerations on cheeks
- Hypoplasia of nails
- Dystrophy of nails
Dysplastic type of Down Syndrome

Severe strabism with general weakness of connective tissue
Down Syndrome

- Loss of control of facial mimicry and motor function in ‘erethic’ type of Down Syndrome
- Salivation dermatitis
- Mimic distortion in ‘erethic’ type of Down Syndrome
Down Syndrome

Chondrodysplastic type of Down Syndrome.
Note the deep-rooted nose and high ‘balcony-shaped’ protruding forehead.
Chondrodysplastic type of Down Syndrome

Note the short arms, especially the upper arm (humerus); also note the short thighs (femur), and short trunk, and the relatively large head.

Physiognomy of a ten year old male after three and a half years of treatment (beginning at the age 6.5 years)
Down Syndrome

Turner type of Down Syndrome. Pterygium colli; “clown cheeks” due to heart defect with mixed cyanosis.

Typical appearance of cheeks due to heart defect with cyanosis. Trophic damage of the skin due to low blood circulation and increased capillary fragility.
Cross-section of physiognomies of two small children that arrived on the same day for pre-cell transplantation examination.
Down Syndrome

Family likeness of treated Down syndrome child with her sibling (see facial angle and hair)

Family likeness of treated Down Syndrome child with her sibling
Down Syndrome

Disturbance of membrane function of oral epithelial cells in Down Syndrome.

Dense bacterial growth on epithelial cell membrane.

Concentration of unspecified esterase (Loeffler Pigmentation) on cell membrane.

Thickening of cytoplasmic membrane.

Thickening of nuclear envelope. Nucleic acid pigmentation with methylgreen-pyronine. RNS = pyrone red; DNS = methyl greenish-blue. The cell membrane is brightly illuminated.
Down Syndrome

Membrane malfunctions of epithelial cells of oral cavity

- Break-up of granulocytes with ‘spikes’ in blood
- Loosened structure of nucleus of monocytes
- Compression of nucleus of granulocytes
Down Syndrome

Calcification of cervical plexus in both lateral ventricles:
(13 ¾ years old Down syndrome male)
Down Syndrome

Diffused and spotted calcifications of diencephalon: 12 3/4 years old male.

Thick skull, high calcium content: 18 years old Down Syndrome female.
Profile of skull size deficiency (shaded area) of an eleven year old mongoloid male. At the end of the physical development, the skull size deficiency amounts to an average weight of 250 grams (= -20%).

*Disproportionate ratio* between large the mid face (viscerocranium) and the small, short skull (neurocranium)
Down Syndrome

Section 1: Length of anterior cranial fossa

Section II: Height of skull above the sella turcica

Sketch of measurements, including measurement points, sections (I-X), and angles (a-ℓ)
Down Syndrome

Section III: Length of posterior part of the skull

Section IV: Posterior cranial base

Section V: Overall length of skull

Section VI: Overall height of skull

Section VII: Overall lateral diameter of skull
Down Syndrome

Section VIII: Depth of facial bone (viscerocranium)

Section IX: Depth of lower jaw.

Section X: Height of facial bone (viscerocranium).
Down Syndrome

Angle a: Inclination of anterior cranial fossa
Down Syndrome

Angle $\beta$: Angle of anterior cranial cavity
Down Syndrome

Angle $\delta$: Angle of posterior cranial fossa
Down Syndrome

Schematic view of diencephalon, hypothalamic centers, hypophyseal stalk, and pituitary gland

Functional interrelationships between the nerve fibers of hypothalamus and the portal vein system of pituitary. Note how the nerve cell secretions are directly dispensed and turned into hormones.
Physiognomy of a 13 1/2 years old Down syndrome male. Note hypoplasia of the mid face.

Down syndrome pelvis: Note the broad iliac wings, flat acetabular roof, steep positions of the femoral necks, as well as slender skeleton of the lower extremities.
Forms of shortness of middle phalanx of fingers (*brachymesophalangia*), a symptom that occurs in approximately 50% of all Down Syndrome patients. The shortened 2\textsuperscript{nd} phalanx of the little (‘fifth’) finger is often combined with a hook-like inward contortion of the shortened little finger (clinodactyly).
Down Syndrome

Shortened hand (brachycarpy), hook-like contortion (clinodactyly), and shortened middle finger bone (brachymesophalangia) of a 17 years old Down syndrome female.

Shortened finger tips (acromicry) [see arrow], hook-like contortion (clinodactyly), and shortened 2\textsuperscript{nd} phalanx of the little finger (brachymesophalangia) of a six years old Down syndrome male.
Mild form of Down-Heart-Syndrome: a combination of various defects of the cardiac septum or heart partitions (here between ventricles, atrium, aorta, and pulmonary artery)

Severe form of Down-Heart-Syndrome: joint opening of both atriums within the ventricles (ostium atrioventriculare commune)
X-ray of mild form of Down-Heart-Syndrome. Note the defects of heart partitions, signs of stress on the right side, and pulmonary hypertension.

Clasp knife phenomenon: A sign of extreme weakness of connective tissues; note the rigid and spastic of joints.
Down Syndrome

Immunoglobulin

Immunoglobulin M

Immunoglobulin A
Down Syndrome

Immunoglobulin

Complement factor C₄

Complement factor C₃

Immunoglobulin G
Down Syndrome

Trisomy 21: There are three chromosome No. 21

Low row third group from the left.

Close-up of three chromosomes No. 21 in lower row on the left.
Body length, mean values, boys \((n=1546)\). There is no significant difference in body length between treated Down syndrome boys \((n=981)\) and untreated boys \((n=565)\) up to age 10. Untreated Down syndrome boys can expect to reach a final body length of 148-151 cm; the mean value of treated boys is around 161 cm, i.e. in the middle between untreated Down syndrome boys and average, healthy boys (174 cm).
The mean body length values of treated Down syndrome girls (n=758) are consistently slightly above those of untreated girls (n=423). The final difference between the two groups is 6 cm. Treated Down syndrome girls reach a final body length of 146 cm, compared to 140 cm for untreated girls, and 166 cm for healthy girls. The effect of treatment on body length is noticeably lesser with girls than boys.
Body weight, mean values, boys ($n=1561$). The body weight of treated and untreated Down syndrome boys between the ages of four and nine years is below the average values for healthy boys in the same age group. After this age group, the body weight of Down syndrome boys is on average somewhat higher than that of comparable age groups of healthy boys. Although a graphic representation of the weight difference is not substantial, in reality the difference is more significant because Down syndrome boys are generally shorter – and thus relatively heavier - than their same-age healthy counterparts. At the end of the somatic growth period, the mean body weight values of treated, untreated, and healthy boys are relatively close. However, due to the shorter body length of untreated Down syndrome boys, they are overweight when compared to treated Down syndrome boys.
Body weight, mean values, girls (n=1203). The body weight of treated and untreated Down syndrome girls up to age 9 is below the norm, whereby the mean values of treated girls is closer to the norm than those of untreated girls. After age 9, the mean body weight values tend to align themselves among all groups. However, it should be taken into account that the shorter body length of Down syndrome girls often results in relative overweight. Moreover, since the body length of untreated Down syndrome girls is shorter than that of other comparable age groups, there is statistically an unambiguous weight gain.
Head circumference averages, boys (n = 1556). The group of treated Down syndrome children (n = 985) shows already from the 3rd year of life higher averages compared with the group of untreated Down syndrome (n = 571), that has after the 10th year of life a larger skull width. At the end of the body growth, the head circumference averages are in untreated 51.5 cm, with treated Down syndrome 53.1 cm, as compared with an average of 54.3 cm with healthy children.
Head circumference averages, girls (n= 1190). The group of treated Down syndrome girls (n=757) shows from the 5th year on significantly higher numbers as compared with untreated group. With increasing age, the difference becomes larger, with considerable variation, more so in untreated group. At the end of the body-growth, head circumference average of untreated Down syndrome girls is 49,5 cm, of treated Down syndrome girls 51,5 cm, of normal girls 54,1 cm.
T test of body length of girls: comparison between untreated and treated children of the same age.
T test head circumference in boys: comparison between treated and untreated children of the same age
T test of body weight in boys: comparison between treated and untreated children of the same age
Macroglossia, with cracked surface, often combined with cheilosis

As early as 20 – 40 minutes after an intraperitoneal injection, there is a noticeable reduction of foreign tissues (hypothalamus, bright scattered cell fragments), disintegration of phagocytes through microphages, or fixation on cell membranes.
Three-dimensional fetal skull quotient (n=100 children, where ● = boys, and ○ = girls). The majority of measured values fall clearly below the norm. It is evident that the fall below the norm begins at 12 months of age.
Three-dimensional fetal skull quotient (n=200 mongoloid children, including 100 cases shown in Fig. 189; ● = boys, and ○ = girls). After the second implantation of fetal brain tissue, the skull index is within the normal range.
Distinct patterns of three-dimensional skull indexes in 20 Down syndrome children (● = boys, and ○ = girls). If the average age is fixed at 100% respective of the norm (horizontal line at 100), then the distinct patterns show the specific responses of fetal skull growth volumes to various combinations of implanted cell transplants of various parts of the brain. The first implantation is shown as a circle, the second implantation is shown as a triangle, and the third implantation is shown as a square. The shaded geometric figures represent males, the blank geometric figures represent females.
Broad dispersion of three-dimensional fetal skull indexes with predominantly negative values before the first implantation; after the second implantation, there is an almost perfect, normal distribution of measured values (n=200 Down syndrome children; \(|=\) before the first implantation; \(\cong=\) after the second implantation).
Increase of the three-dimensional fetal skull index in extremely microcephalic Down syndrome children (Starting values below -6% of the norm; n=50); after the first implantation of lyophilized fetal tissues – in each case 200-300mg – there have been considerable increases in volume in the majority of cases; there has also been a substantial approximation to the mean values of the norm (=±0%). Many cases have achieved positive values.
Motivation for language acquisition to meaningful words: Guide for parents. Imitating movements. Imitating specific body movements can help in teaching a relationship between movement and language. If the child does not react spontaneously, the mother can take the child’s hand in guidance. Nursery rhymes or children songs can be accompanied with appropriate movements.

Music (from radio or music CDs) can be used to teach (a) rhythmic swinging of arms (Fig. 203), (b) stretching of arms, clapping of hands (Fig 204); (c) stomping of feet, jumping, etc. (Fig 205). The mother demonstrates each movement, and encourages the child to imitate each movement.
Imitating games

Building blocks can be arranged in various sizes and forms; this can help to develop attention span and concentration. The child also learns to take on and complete a task – a precondition for later scholastic and other activities.
Position for feeding

1. The child sits with bent legs on the mother’s lap

2. The child’s back and head are supported by a cushion or back of the chair

3. The mother can see the child and, if necessary, close the child’s jaws and lips
Exercises for the mobilization of mouth muscles 1

1. The mother strokes the child’s mouth region with both index fingers in the direction of the lips.

Exercises for the mobilization of mouth muscles 2

1. The mother forms the child’s lips into a round position
2. The child is encouraged to produce the /u/ sound (as in “put”)
Down Syndrome

**Exercises for the mobilization of mouth muscles 3**

1. The mother uses slight pressure to open and close the child’s lower lip
2. The child is encouraged to produce the /a/ sound (as in “father”)

**Exercises for the mobilization of mouth muscles 4**

1. The mother closes the child’s lips
2. The child is encouraged to produce the /m/ sound
3. The child is then encouraged to produce combined sounds (m-ah, u-ah, u-m, etc.)
Down Syndrome

**Exercises for the tongue 1**

1. The mother massages the tongue with a finger or small spoon in circular motion

**Exercises for the tongue 2**

1. The mother pushes the tongue with a finger or small spoon to the left and right
1. To promote the sticking-out of the tongue, the mother can put small quantities of jam or chocolate on the child’s lips.
2. This also promotes a licking movement.

**Exercises for the tongue 3**

1. During the licking movement, the tongue is pushed upwards and downwards.

**Exercises for the tongue 4**
1. To encourage chewing, the child eats with a spoon.
2. The mother closes the lips of the child.

**Chewing exercises 2**
1. The mother holds the child’s head from behind.
2. The mother moves the child’s lower jaw up and down.
3. After two or three movements, the lips are pushed together once more.
4. This exercise must be repeated several times.

Try to start spoon-feeding the child as early as possible (week eight after birth).
Down Syndrome

Sitting position (when eating)

1. The child’s legs must be placed firmly on the ground
2. The table height must be adjusted so that the child can extend his/her arm on the table (shoulder and arms reach forward)
3. If possible, put plates on slip-proof place mat.
1. To prevent chewing when drinking, the mother stands behind the child and holds the lower chaw with one hand, and the cup with the other hand.

2. If able, the child can hold the cup with both hands, and rest the elbows on the table.

3. Eating and drinking should be done in a relaxed atmosphere.

**Sitting position (when drinking)**
Painting and drawing by Down syndrome children: Rudimentary use of colors and shapes up to and including simple landscapes (from age six to nine). Note the representation of sun rays in spectral colours.
The cheerful view of the world of eight year old Marcus is expressed in colours and themes; the ship heading for the port of Amrun is colourful; the meadow is full of experiences. During a hospital visit, he gets stuck in the elevator (lift).

The experience of being stuck in an upward-moving vehicle (note the ladder on the outside) is deeply processed. The sun is not rendered brightly yellow – as in his other graphic representations - but dark; he strongly expresses a wish-dream to find himself on the meadow in this situation.
Trees and flowers are drawn primarily by Down syndrome girls between the ages of eight and 15 years. Note the expressiveness and, in some cases, the precision.

Handwriting: Wishing you a Happy New Year, from Susanne
Creative rendition of festivals and well-wishing events. The Christmas greeting (by 12 year old Rainer) contains all the essential elements; the same goes for the Easter drawing of 13 year old Peter, and the New Year’s wish of 10 year old Susan.

The Easter egg (by 14 year old Martina, Fig. 316) is rendered in bright colors; the carnival scene (by 11 year old Sylvia) is lively and expressive.
The selected animal scenes disclose subtleness in their respective representations, such as 13-year old Martina’s squirrel, giraffe, and deer, and 11-year old Brigitte’s bird. The beetles are a collage of coloured paper and glue.
The graphic rendering of actions moves between abstractness, essential, and playfulness. The laughing tea pots, drawn by a 15 year old, disclose the same kind of humour that he also draws in the faces of locomotives.

Fourteen-year old Klaus-Peter occupies himself not only with the drawing of technical problems (bus, ski lift) but also with action drawings such as the bridal pair in church, and at the house entrance.

Fourteen-year old Jürgen uses playful colour combinations in the “Bounty”, and drama in “Jesus as Fisherman”.

Fourteen-year old Martina displays good observation skills in the “ski slope” drawing.
Handicraft abilities of Down syndrome children from age 10 – 18 years
The Use of Fetal Precursor Stem Cell Therapy in the Treatment of Age-related Diseases and Chromosomal / Genetic Diseases in Patients
Official medicine declared ageing a natural inevitable process: there is no such thing as an ‘ageing disease’, and thereby no reason for any R&D, as there is nothing that you can do against ‘Mother Nature’.

World Health Organization Study Group on Aging and Working Capacity, Helsinki, Finland, 1991, analyzed all issues thoroughly and advised governments on problem areas, but there was no discussion how to handle ageing therapeutically.

Clear message to the ageing population world over: ‘the moment you stop working you are becoming a financial burden on government, so why to waste money on therapies of the ageing disease’.

Today all governments are asking workers to postpone retirement.

Over 4 million patients treated worldwide for ‘ageing disease’ by cell transplantation / cell therapy during the last 75 years has disagreed with the politicians. They reached in their pocket not add years to their lives, but to add life to their years.
The goal of medicine is to learn why aging takes place, and to discover treatment to *preserve the vitality of aging organism for as many years as possible, ideally until the alleged limit of our life of 120 years.*

Vitality measures the ability of one’s organism to realize all vital functions in physical, mental and spiritual spheres.

Vitality is an optimal performance of capacities existing in an individual.

‘Devitalisation’ means loss of vitality due to aging disease, and aging-related diseases.

‘Revitalisation’ means re-establishment of lost vitality,

while ‘rejuvenation’ goes beyond that, it improves one’s total biological capabilities, and lowers the biological age.

From our empirical knowledge, based on treatment of millions of patients with aging disease by cell transplantation over the last 75+ years, compensates for inadequacy of medical science.
Ageing and lifespan are genetically determined. Genes are the sole entities in Nature that never die: the expression of genes changes with aging, not with their content. Patients with genetic diseases with shortened lifespan are considered a proof of the theory: Down syndrome, Klinefelter syndrome, Turner syndrome, progeria, Cockayne syndrome, ataxia telangiectasia, Seip syndrome, myotonic dystrophy.

Blueprint of all organs, tissues, cell types, and their function is coded in nuclear DNA.

Negative balance of repair vs DNA damage causes ageing process. At autopsy of adult Down syndrome patients morphological and histochemical changes typical of Alzheimer disease are found in the brain.

Studies of monozygotic twins showed that 2/3 of lifespan variability is not of genetic nature.
2) Theory of ‘Death Hormones’,

When an internal ‘ageing clock’ signals a pre-set alarm launching the ageing process, in response, key organ systems in our body begin to decline.

Such ‘ageing clock’ could be located:

- in the regulatory center, e.g. in thyroid, pituitary, hypothalamus,
- in each cell, in the same part of a cell as is the reproductive blueprint, i.e. in DNA.

As errors of DNA replication accumulate, and thereby causing gene expressions to deteriorate, the ageing disease progresses.

All remaining theories point to the environmental cause of ageing.
3) Theory of neurotransmitters -

Neurotransmitters are biochemicals that make transmission of impulses between neurons possible. Everything CNS does is a matter of neurotransmitters' allowing impulses to cross synapses between neurons.

If these substances are not supplied and distributed in adequate amounts, the brain malfunctions. As the brain is the control center, the function of other organ systems of the body deteriorates as well.

With age, concentrations of neurotransmitters, and their distribution throughout various parts of CNS change. *Balances between catecholamines and serotonin maintained for four decades falter.*

Chemical environment of CNS starts to shift, slowing down the processing speed of ‘our’ computer.
4) Autoimmune Theory of Ageing

With aging, ‘immunological memory’, which is vitally important for the function of immune system, begins to work against us: immune system will lose its ability to distinguish ‘self’ from ‘non-self’ and begins to attack the same body it must protect.

Lymphocytes retain ‘autoimmune memories’ against the body they are supposed to defend. Once a lymphocyte has an autoimmune memory, it is useless against real infectious threats to the organism.
Free radicals are molecular fragments with an unpaired electron in its outer electron ring that causes molecular fragments to be highly unstable, eager to trigger reactions with many substances in the vicinity, particularly oxidative ones.

It takes only one millionth of a second for a free radical to interact with nearby molecules, trigger chain reactions, and cause damage to various components of a cell, and ultimately cell death.

Each uncontrolled free radical can multiply up to a million times, like in a nuclear fission reaction.

Free radicals are formed in our bodies in two ways: by design and by accident.
6) Theory of Cross-linking (linked to 5).

Cross-linking are bonds between molecules that are normally not bound together.

Formation of chemical bridges between normally free molecules progresses slowly for a long time before causing damage. *Cross-linking strikes large molecules, such as proteins and DNA.*

During young age, the body produces enzymes that break down excessive cross-linking immediately.

With ageing, cross-linking will develop at an increasing rate, because the broken down enzymes are not synthesized with sufficient speed.
Impaired blood flow due to atherosclerosis causes faster cell deterioration and slower cell repair.

If blood flow to an organ is restricted, many cells are not repaired, the organ malfunctions, or fails to function, and begins to die.

If the organ is vitally important and artificial organ or organ transplantation is not available, the organism dies.
The end-products of metabolism of each cell of the body must be regularly removed as otherwise build up of such waste in lysosomes will cause the cell malfunction and eventually death.

Lysosomes overfilled with dangerous substances burst: they are ‘suicide bags’ of cells.

8) Accumulation Theory of Ageing
There are two major types of 'ageing disease':
- accidental or random, and
- programmed
because we age 'by accident’ and ‘by design'.

Not only wear and tear of everyday life sets off processes that make us grow old, there is some internal mechanism that limits our lifespan. Our evolutionary biological purpose is fulfilled after we passed on our genes, and protect our children until they can defend themselves. Once that happened, around the age of 40, we notice the ageing process.

Before that time our bodies were in a state of dynamic equilibrium, constantly renewing, rebuilding, and replacing every cell in the body by cells of equal quality.

Now our physiological functions begin to deteriorate. Our ability to adapt to, and survive in a changing environment, declines. The whole body, the structure of tissues becomes disorganized.
The latest “Merck Manual of Geriatrics” defines

‘usual ageing’ - 'changes due to the combined effects of the ageing process and of disease and adverse environmental and lifestyle factors', while 'successful ageing' - 'changes due solely to the ageing process, uncomplicated by damage from environment, lifestyle, or disease'. These definitions acknowledge the possibility of 'ageing successfully'.

‘Usual ageing’ should be defined as ‘ageing disease’, and all diseases related to ageing clearly described.

Scientists agree that genetically we are programmed to live 120 years. Today we live on average less than 80 years in the civilized world.

There are societies with simple lifestyle where people live frequently much longer than that.
Successful ageing process leading to our demise at the age of 120 years, is disrupted by three factors:
- severe illness,
- severe trauma, or
- ‘usual ageing’, i.e. ‘ageing disease’.

The first two factors are self-explanatory: severe disease or severe trauma can destroy even the healthiest individual.

What about ‘ageing disease’?
Some well established facts:
1) The rate of age-related decline in the function of every organ varies greatly, so that people become less alike as they age;
2) Within any organism the functions of various organs decline at different rates;
3) Each one of us has at least one weak organ or organ system;
4) Different people age at different rates, and the pattern of their ageing varies, as well.
Medicine cannot successfully treat ageing related diseases, or other diseases in an ageing patient, without treatment of ageing disease.

Results of treatment of ageing disease, or 'revitalisation' / 'rejuvenation' therapies, will be decreased significantly without a ‘state-of-art’ - diagnosis of any and all diseases that the patient suffers from, and - in-depth evaluation of the functional state of all organ systems.

There are not too many 40+ years old individuals in the civilized world today that are perfectly healthy physically, mentally and spiritually, that do not require treatment of 'ageing disease'.

The earlier in life revitalization therapy program is begun, the better are the results. The best time to start is between 40 and 50 years of age.

The later the revitalization program commences, the more aggressive has to be the therapeutic approach, i.e. it is mandatory to carry out - various therapies simultaneously, and - more frequently.
For an early diagnosis, and evaluation of therapeutic results, *detailed lists of ‘devitalisation’ symptoms & signs* were devised, such as of F. Schmid.

**‘Social behaviour / Psyche’:**
- Discontent,
- Self-reproach,
- Loss of interpersonal relations,
- Fear of living,
- Desire to live like a hermit,
- Loss of interest in sports, politics, acquaintances, environment, hobbies.

**‘Personality’:**
- Loss of initiative,
- Lack of vigour,
- Emotional ‘emptiness’,
- Lack of inspirations,
- Feeling of insecurity,
- Egocentric behaviour,
- Inability to act,
- Loss of sanity.
List of ‘devitalisation’ symptoms and signs of F. Schmid (cont’d)

‘Gross motor abilities’:

• Rigid posture,
• Unsteady gait,
• Shuffling walk,
• Reduced walking distance,
• Difficulties to climb stairs, walking with walking aid

‘Fine motor abilities / Coordination’:

• Reduced mimicry,
• Reduced gestures,
• Tremor,
• Shakiness,
• Unsteady grip,
• Restlessness.
List of ‘devitalisation’ symptoms and signs of F. Schmid (cont’d)

‘Intellectual performance’:
- Impaired comprehension,
- Impaired intellectual grasp,
- Memory disturbances,
- Loss of short-term memory,
- ‘senseless’ mistakes,
- Reduced concentration,
- Reduced vocabulary,
- Loss of contemplation,
- Taciturnity,
- Monotonous stereotypes,
- Loss of orientation abilities.

‘Physical regression’:
- Skin atrophy,
- Vascular sclerosis,
- Cerebral sclerosis,
- Aged heart,
- Pulmonary emphysema,
- Digestive disorders,
- Impotence,
- Menopause,
- Old-age diabetes, liver disorders,
- Immune deficiency.
Biological age refers to functional capacities of an organism corresponding to the respective stage of individual’s lifespan.

After a developmental phase, and period of maturity, comes period of regression.

Motor, psychological/social, and intellectual skills, acquired during the developmental phase, utilized during maturity, are then gradually lost during the regression period: abilities acquired last are lost first.

Several attempts to create a simple system of assessment of biological age for everyday clinical practice: that of E. Ries includes an evaluation of:

- cardiovascular system, i.e. blood pressure, vital capacity of lungs, partial pressure of arterial oxygen, Ruffier tests of fitness,
- sense organs and psyche, i.e. visual acuity, audiogram, reading ability, color-word-tests of Stroop, speed of movement,
- locomotor system, i.e. power of hand muscles, hand dynamometer, tendon extension in degrees,
- dental status, i.e. number of decayed, missing and filled teeth.
Experts always believed in a complex approach to the treatment of ageing disease, i.e. *fetal precursor stem cell therapy alone is not sufficient.*

The basis are:
- lifestyle adjustments,
- correct nutrition,
- regular active exercise
- proper handling of stress
- spiritual immersion.

Functional normalisation of all organ systems by all means of orthodox and alternative medicine, and detoxification, is the key task for treating professionals.

Two most important parts of the complex therapeutic approach are

- **FPSCT** for direct stimulation of regeneration and

- **FPSCT along with electromagnetic therapy** for optimizing the function of regulatory systems.
FCTI’s COMPLEX THERAPY OF AGEING DISEASES

Level 5
FETAL PRECURSOR STEM CELL THERAPY

Level 4
ELECTROACUPUNCTURE based ELECTROMAGNETIC THERAPY

Level 3
MICROBIAL THERAPY  ENZYMOTHERAPY  CHELATION THERAPY

Level 2
HOMEOPATHY  OXYGEN THERAPY  PHYSIOTHERAPY

Level 1
Nutrition & Diet  Exercise & Fitness  Stress Handling & Mental Hygiene

LIFESTYLE MODIFICATION  SPIRITUAL IMMERSION
1) A patient with ‘ageing disease’ needs an improvement of biological functions in their entirety (i.e. ‘vitality’): physical, mental and spiritual;

2) A follow-up requires measurement of parameters described in therapeutic protocol, but also an evaluation of the ‘vitality’, which to some degree is a matter of the patient’s personal judgment;

3) *The more advanced the symptoms and signs of ageing disease* the more thorough the diagnosis must be for all diseases and malfunctions of all organ systems, and more attention needed during the after-care post-FPSCT;

4) The regenerative ability of an organism is diminishing with age, thus the ‘ageing disease’ needs to be treated earlier, and more frequently. The older the age of patient at the time of the first treatment, the more frequent the treatment should be. *As long as there is some regeneration potential left, and the patient is not in the terminal stage of a disease(s), FPSCT should be an option.*
The revitalization effect of FPSCT, especially of placenta and gonads, has been researched extensively in animal experiment by Kment and his students:

it is less a targeted stimulation of specific organs, and more a general improvement of elementary functions of the entire organism, and thereby increased vitality.

Term ‘revitalization’ was created by Niehans, as he wanted to clarify that ‘rejuvenation’ is not possible since biological clocks cannot be moved backward.

But a discrepancy between the chronological age and biological age is correctible.
Rietschel described the **revitalization effect of cell transplantation as an ‘improvement of the general state of health’**.

Majority of patients suffering from various diseases seldom state that their ‘heart condition, digestive function, or breathing, etc., is better after FPSCT, but **speak of subjectively improved general state of health**, i.e. **patients do not notice the better function of a single organ, even if that organ is malfunctioning and thereby of deep concern to the patient**, but rather a better appetite, or change of taste for more appropriate foods, adjustment of weight, healthier skin color (from better skin circulation), disappearance of wrinkles, stable emotions, more active mental and physical state, i.e. increased vitality.

Physical and psychological factors overlap and are inseparable in patients’ description of their condition.

There are positive changes of metabolism which are the basis of regeneration of damaged organs, and that is what is perceived by the patients as revitalisation.

On the basis of 378 own patients studied, the revitalisation rate of **93.5%** was reported after FPSCT.
Studies on the therapeutic effect of FPSCT on the ageing disease using experimental animals are difficult to do, and there are always questions whether results of such animal studies are of any value to a patient with ageing disease, i.e. does it improve therapeutic options.

Multiple experimental animal studies, carried out in particular by Kment and his group in Vienna, Austria, were based on recognition of:
- close relationship between wear and tear and ageing process; and
- the ties of ageing process to the vitality and various diseases of the older age.

For studies of ageing, wear and tear, involution & lowered vitality, controlled experiments in rats were carried out on:
- elasticity and tear resistance of aorta and skin,
- collagen performance,
- tissue respiration in tissues of aorta, heart, liver, and kidney,
- mitochondrial function of myocardial fibers and hepatocytes,
- spontaneous activity, resorption, distribution, and elimination of V-Penicillin, in relation to age.

FPSCT of placenta and gonads significantly improved all measured parameters.
Others proved that FPSCT improves tissue oxygenation, thyroid function, reverses atrophy of vaginal epithelium, prolongs lifespan, etc., but if all such positive results are gathered together they still give no answer to the key question about vitality.

One can preach after Gallileo Gallilei “to measure what is measurable, and make measurable what has not been measured yet” but vitality still cannot be directly measured.

Medicine is not a pure science but also an art, and we have to trust the wisdom of patients: the repeated FPSCT treatment by millions of patients seeking revitalization by their own volition is a scientific fact like any other.
Female patients should receive as a minimum stem cell transplants of ovaries, placenta, adrenal cortex, hypothalamus, liver, while male patients should receive at least stem cell transplants of testes, placenta, adrenal cortex, hypothalamus, liver.

Stem cell transplants of placenta and adrenal cortex must be from the fetuses of the same sex.

Additional stem cell transplants, necessary for the treatment of patient’s other disease(s) that have a negative influence on ageing disease, are added.
FCTI’s Method of FPSCT Manufacturing
Preparation of FPSCT as “living systems” is a ‘biological’ rather than ‘biotechnological’ process.

‘Biotechnological process’ implies manufacturing of non-living substances by living cells, while ‘biological process’ means manufacturing of live cells for various purposes, incl. cell transplantation.

- Biotechnological products can be standardized, even though inherent variability is unavoidable, and deficiencies are not revealed by final testing.
- Biological products cannot be standardized: impossible to get uniformity and consistency of stem cell transplants from batch to batch.
As long as we do not know what is life, it will be impossible to
- standardize,
- control, and
- validate
the manufacture of FPSCT.
Primary Goals of FCTI FPSCT Manufacturing Method (1)

- to abolish (or minimize as much as possible) immunogenicity of FPSCT, and to simultaneously
- prevent transmission of zoonoses by implantation of FPSCT.

It is accomplished by following procedures of FCTI’s U.S. Patent (U.S. Patent Pending) and related know-how, which is in accordance with appropriate parts of “PHS Guidelines on Infectious Issues in Xenotransplantation” of 1/19/2001 (Federal Register, volume 66, No. 19, pages 8120-1) as well as European Council Directive 001/83/EC, which affirms the decision of German Supreme Court of 2/16/2000 in 1 BvR 420/97, whereby live cell therapy (i.e. cell xeno-transplantation) is still to be permitted in Germany as it has been since 1950’s.
Key step of FCTI Method is a unique procedure of primary tissue culture. While principles are firmly set, preparation of each FPSCT is different:

each tissue culture is handled individually, like a “living being”:

i.e. tissue culture conditions are modified as required by
- growth of colony of cells, and
- cytological features of cultured cells

The ‘prescription for living conditions’ of each tissue culture is made every day by an expert.

In other words, each primary tissue culture procedure varies: FCTI know-how and 25+ years’ of experience prevail in adjustment of utilized tissue culture techniques.
Key Points U.S. FDA Regulation of 1/19/2001

Link between “scheduled” rabbit females from closed colony, identified by numbers given at birth, (source of all fetal and newborn rabbits used in manufacture of stem cell transplants)

and

a patient / recipient of a batch of stem cell transplants necessary for treatment of his/her disease, identified by a code known only by the manufacturer, must not be interrupted throughout the whole manufacturing cycle. IT MUST BE POSSIBLE TO RE-TRACE THE LINK AT ANY TIME IN THE FUTURE!

This is done via stored samples of each stem cell transplant, and via archiving of records (also valuable for liability protection).
1. All stem cell transplants prepared for one specific named patient are classified as “batch”.

2. All stem cell transplants in a batch are prepared from fetuses and newborns of pre-scheduled rabbit females only!

3. Each sterilized box (for transportation between rabbit colony and manufacturing laboratory) contains only one ‘pre-scheduled’ rabbit female, to be used as source of fetuses, marked by identification number of that rabbit female. Each sterilized ‘small’ transportation box contains only newborns of one pre-scheduled rabbit female, marked by an identification number of that rabbit female. All ‘small’ boxes with rabbit newborns necessary for manufacturing of a batch of stem cell transplants for one named patient are placed inside of one large card box.
4. All ‘source’ animals are processed in groups. One “group” equals all fetuses of one rabbit female or all newborn rabbits from one small box, i.e. from one female.

5. All euthanized animals of one group are placed in a metal container marked with an identification number of a rabbit female, ‘source’ of all fetal or newborn cadavers in the metal container.

6. Dissecting pathologist places all organs and tissues necessary for manufacture of each FPSCT of a batch in Petri dishes marked with:
   - the name of FPSCT prepared,
   - identification numbers of all rabbit females, ‘sources’ of fetal or newborn cadavers, and
   - code of a patient / recipient of a batch of FPSCT.
7. During the manufacture, each tissue culture flask is marked with
   - the name of stem cell transplant
   - identification numbers of all rabbit females, ‘sources’ of
     fetal and newborn cadavers
   - patient / recipient’s code

8. Each transportation vial contains the full individualized treatment dose of
   one stem cell transplant of a batch labeled with...
   - name of manufacturer
   - name of FPSCT
   - batch number
   - patient’s code
   - identification code of FPSCT
9. This code is linked to all fetal and newborn rabbits used in the manufacturing of a FPSCT placed in that vial via the identification numbers of all females, ‘sources’ of the same fetuses or newborns as well as to the:

- detailed records of entire manufacture,
- records of histological verification of the organ or tissue origin of each stem cell transplant,
- records of microbiological testing,
- records of bacterial endotoxin test,
- records of other tests for quality control and validation.
Fetal and newborn rabbits used for preparation of FPSCT originate from closed colony of rabbits, with documented lineages for >3 years (>20 generations), breed and reared in captivity, and not exposed to vectors of infectious agent.

In order to qualify as a source of fetal and newborn rabbits to be used for preparation of FPSCT a rabbit colony has to
• be a closed colony as per guidelines of WHO and AAALAC
• have an adequate surveillance program for infectious agents for >3 years (if less than 3 years, then immunological assays for all known infections of rabbits were carried out – and were negative)
• avoid use of live attenuated vaccines.
Guidelines of WHO and AAALAC for closed colonies consist of:
- criteria for new rabbit admission
- disease monitoring program
- criteria for isolation and elimination of diseased rabbits
- criteria for health screening of all humans in contact with rabbits
- facility cleaning procedures
- source & delivery of feed, water, supplies
- exclusion of arthropodes and vermin
- transportation of rabbits
- dead rabbit disposition

Hormonal stimulation for impregnation must be avoided if fetuses / newborns are to be used for manufacture of FPSCT.
Animal Source of FPSCT (3)

The movement of rabbits is always “one way”, i.e. “all in - all out”:

- Proper number of rabbit females is ‘pre-scheduled’ to deliver within 24 hours prior to the start of manufacturing of a batch of FPSCT.
- One female (source of fetal rabbits) is removed from closed colony one - two days before delivery date and taken to the manufacturing laboratory in a sterile box.
- Newborn rabbits delivered by remaining ‘pre-scheduled’ females during 24 hours prior to the start of preparation of a batch of cell transplants are taken in sterile boxes to the manufacturing facility.
- No rabbit taken out of closed colony is ever returned back.
Screening for Infectious Agents Before and During Manufacture of FPSCT (1)

- continuous and documented evaluation health status evaluation of the entire closed colony with certified pure lines of rabbits, all identified & marked by number since birth
- continuous evaluation of all ancestors (for at least 3 generations) of ‘pre-scheduled’ rabbit females, ‘sources’ of all fetal and newborn rabbits needed for manufacture of a batch of stem cell transplants, marked by a number
- continuous health status evaluation of ‘pre-scheduled’ pregnant rabbit females
- health status observation of fetal and newborn rabbits
- daily macro- and microscopic evaluation of each primary tissue culture;
Screening for Infectious Agents Before and During Manufacture of FPSCT (2)

• final assay of each FPSCT by
  a. histological evaluation (microbes seen too)
  b. bacteriological testing
  c. bacterial endotoxin test

UPON ANY SUSPICION THAT A PRIMARY TISSUE CULTURE IS NOT IN PERFECT CONDITION WILL BE IMMEDIATELY DISCARDED!
(since there is time restriction for investigation)

IMPORTANT POINTS:
• epizootiology of country of manufacture must be known in detail
• in civilized world pathogens are found in adult rabbits only (NOT USED BY FCTI), i.e. no pathogens in newborn rabbits
• fetal rabbits are sterile
• no retroviruses found to-date in rabbits!
Screening for Infectious Agents Before and During Manufacture of FPSCT (3)

MONITORING OF CLOSED COLONY FOR INFECTIOUS AGENTS THAT ARE NOT APPARENT `CLINICALLY`:

ALL ADULT RABBIT FEMALES SERVE AS "SENTINEL ANIMALS" OF ANY NEW INFECTIOUS AGENT OR DISEASE NOT KNOWN OR SUSPECTED TODAY.

All adult rabbit females are examined at the beginning of a breeding cycle, and every 6 months thereafter, by DVM and

1. blood samples (serum, and leukocytes) to be kept in liquid nitrogen for 5 years for future microbiological testing
2. specimen for blood count and peripheral blood smear
3. specimen of feces to be tested for parasites
4. nasal swab for microbiological culture are collected and after death all adult rabbit females are subjected to a full autopsy, and samples of blood, liver, spleen, bone marrow and brain are obtained, to be stored for 5 years for future testing.
Carried out under aseptic conditions following GMP rules:

- Full autopsy of each fetal and newborn rabbit is carried out by a veterinary pathologist, who - if findings are normal - then collects all organs and tissues necessary for preparation of a batch of FPSCT.
- In case of pathological findings the source animal is discarded.
- Autopsy report is a part of a record of each FPSCT.
- At the final step of manufacturing process - collection of cultured tissue fragments into transportation vials - three samples of supernatant of each FPSCT are taken:
  - 1st sample kept by manufacturer in liquid nitrogen for 5 years
  - 2nd sample used for microbiological testing
  - 3rd sample used for bacterial endotoxin test
Before release of a batch of FPSCT all documentation about manufacturing is checked by quality control unit. This includes description of:

- all steps of manufacturing process
- all components, supplies, containers, closures, labels, etc.
- all post-manufacture testing and sampling, including storage of the last supernatant of each tissue culture flask
- all other data required by GMP

All documents signed by the supervising doctor / tissue culture expert, co-signed by the manager.

The following is essential for the safety of FPSCT as a treatment method, because it allows a retrospective investigation or containment of suspected new xenogeneic infection.
Archiving of records - allowing accurate linkage between

- medical records of named recipient of FPSCT
- release records of each FPSCT used for treatment
- status records of frozen specimens of last supernatant of tissue culture flasks of each FPSCT of a batch
- autopsy records of each rabbit female whose fetuses or newborns were used for FPSCT of the patient
- health data of the closed colony of rabbits, containing:
  1. record cards posted on cages of each rabbit female, with ID numbers;
  2. autopsy report of each female
  3. records of all incidents affecting the health of the colony (diseases, sudden death of rabbit(s), environmental breaks, etc.)
  4. records of all colony health surveillance programs all of the above linked to the code of each FPSCT as it appears on its label.
Labels on a box containing a batch of FPSCT to be used for treatment of a specific named patient include following data:

(a) Name & address of manufacturer: Fetal Cell Technologies International Inc, Laboratoires Dom AVMM (Suisse) Inc, Leutschenbachstrasse 95, 8050 Zurich, Switzerland

(b) Names of each FPSCT in the batch stating from which organ or tissue each FPSCT originates

(c) Batch number

(d) Patient’s code

(e) Identification codes of each FPSCT in the batch

(f) Volume of each FPSCT of the batch – “dosage”

(g) Description of supernatant

(h) Release date

(i) Statement: “Expiration date: 7 days from release date, if maintained at room temperature at all times, but implantation within 48 hours advised!”

(j) Statement: “Recommended storage temperature: 20 degrees Celsius”

(k) Statement: “Live cultured tissue fragments! NO PRESERVATIVES USED!”

(i) Statement: “Route of administration: Implantation by specialized injection techniques as per enclosed instructions”

(m) Statement: “HANDED TO THE PATIENT’S PHYSICIAN ONLY!”
a. Name and address of supplier:
   Fetal Cell Technologies International Inc
   Laboratoires Dom AVMM(Suisse)
   Leutschenbachstrasse 95, 8050 Zurich, Switzerland

b. Names of each FPSCT in the batch stating from which organ or tissue each FPSCT originates

c. Batch number

d. Patient’s code

e. Identification code of each FPSCT in the batch;
   will also appear on the label of the vial of each FPSCT of the batch.

A delivered batch of FPSCT is accompanied by specific instructions about implantation sites of each FPSCT.
FCTI Fetal Precursor Stem Cell Therapy are:

- readily isolated, cultured and stored
- usable without immune-suppression due to culturing process producing
- negligible low antigenicity
FCTI’s Closed Colony Rabbits
FCTI’s Closed Colony Rabbits
Type 1: M91 (origin in 1991)

This Nitra special rabbit lines (population) are directed for meat production and laboratory exploitation in biological R&D in Stem Cell Xenotransplantation. Each line is genetically homogenous and both are under permanent veterinary control.

M91 are bred for good manifestation of mother utility traits (e.g. conception rate, litter size, lactation, etc).
P91 is a typical paternal line (for production breeding males) with good growth of live weight, feed conversion and meat utility traits.
Rabbit used in biology experiment are free from:

Bordetella bronchiseptica, Cilia-associated Respiratory Bacillus, Clostridium piliforme, Encephalitozoon cuniculi, Rotavirus, E. coli.

Good stalling (keeping) conditions are necessary for good health status of animals (fig 4). Stainless steel metal cages, adjusting of microclime conditions (temperature, humidity, air draught, photoregime, concentration of toxic and irritable gases etc.) and optimalisation of food nutrients in pellets are essential for good results.
Organization of rabbit breeding in controlled reproduction system (1)

The reproduction phase of production will be realized on the basis of controlled reproduction.

For reproduction, female rabbits will be used at minimum age of 17 weeks and weight minimum 3.5 kg. At selection, stress will be laid on good state of health and efficiency of parents.

Artificial insemination procedure

Automatic feeding tubes
Basis of controlled reproduction will be artificial insemination. Preparation of female rabbits on insemination will be divided into three phases:

A. synchronization and maturation of follicles,

B. collection of semen, control, preparation of insemination doses,

C. application of insemination doses, stimulation of ovulation.

Employees on the farm will perform the whole process of controlled reproduction.
THE EXPERTS IN STEM CELL TRANSPLANTATION SINCE 1991

- Fetal and precursor stem cells of any of the known cell types as required
- Lesion repair using same type of cells as lesion
- Genetic Diseases
- Chromosomal Diseases
- Neoplastic Diseases
- Central Nervous System Diseases
- Endocrine Diseases
- Kidney Diseases
- Lung Diseases
- Renal Disease
- Treatment of Radiation Injuries
- Muscular Dystrophy
- Huntington's Disease
- Cystic Fibrosis
- Cerebral Palsy
- Spinal Cord Injury
- Multiple Sclerosis
- Muscular Dystrophy
- Brain Tumors
- Cancer Treatment
- Sickle Cell Disease
- Rheumatoid Arthritis
- Osteoarthritis
- Autoimmune Diseases
- Inflammatory Bowel Disease
- Diabetes
- Colitis
- Ulcerative Colitis
- Crohn's Disease
- Liver Diseases
- Liver Disease
- Cardiovascular Diseases
- Liver Cirrhosis
- Gallstones
- Biliary Atresia
- Atherosclerosis
- Congenital Heart Disease
- Aneurysm
- Neurofibromatosis
- Skin Diseases
- Dermatitis
- Eczema
- Psoriasis
- Burn Scars
- Vitiligo
- Wound Healing
- Fibrinogen Deficiency
- Hemoglobinopathies
- Red Blood Cell Disorders
- Thalassemia
- Sickle Cell Disease
- Immune System Diseases
- Immunodeficiencies
- Autoimmune Diseases
- Immune Reconstitution Inflammatory Syndrome
- FCI's Fetal Precursor Stem Cells

www.fetal-cells.com
BRAIN INJURY
FCTI Fetal Precursor Stem Cell Transplants
.... the solution

Brain injury occurs when either the nerve cells or nerve pathways are broken, compressed or starved of a blood supply. This can happen as a result of mechanical force, insufficient blood reaching the brain tissue, infection, chemical poisoning or by a tumour. The brain acts as a central centre for movement, sensation, emotion, behaviour, intellectual function.

The Brain
- Parietal Lobe
  - Perception, sensory situation
- Frontal Lobe
  - Intellectual function, behaviour, personality, all muscular movement
- Occipital Lobe
  - Vision
- Temporal Lobe
  - Speech, hearing, memory
- Cerebellum
  - Balance

CANCER
FCTI Fetal Precursor Stem Cell Transplants
.... a new concept in treatment of cancer

Cancer is a group of many related diseases that begin in cells. Normally, cells grow and divide to produce more cells of the same type in order to replace cells lost due to normal wear and tear. Cancer cells grow abnormally and keep dividing in forms cells without control or order, creating a mass of abnormal tissue called a tumour. Tumours can be malignant (cancerous) or benign (non-cancerous). The cells in malignant tumours can invade and damage normal tissue and organs. Cancer cells can also break away from malignant tumours and travel through the bloodstream or lymphatic system to form new tumours in other parts of the body, i.e. metastasis.
CEREBRAL PALSY
FCTI Fetal Precursor Stem Cell Transplants
... the solution

Cerebral Palsy is caused by damage to the developing brain usually occurring before, during or shortly after birth. Brain damage can also occur during infancy due to infection or trauma.

Types of Cerebral Palsy

- Spastic
- Athetoid
- Ataxic
- Flaccid

Diabetes Mellitus
FCTI Fetal Precursor Stem Cell Transplants
... the only approach

Diabetes mellitus is a disease of the Langerhans islets of pancreas. In type 1 diabetes the insulin-producing beta cells of the pancreas are destroyed by the immune system. Patients with type 1 diabetes produce insufficient quantity of insulin. Unlike in type 1 diabetes, patients with type 2 diabetes produce insulin however the body is unable to recognize insulin or use it properly.

Complications of Diabetes Mellitus

- Retinopathy
- Nephropathy
- Polyneuropathy
- Vasculopathy
- Brittle diabetes of children
- Diabetes in females infertile, frequently spontaneously aborting, or delivering dead babies, and newborns with diabetic syndromes

Oesophagus
Islets of Langerhans
Duodenum
Pancreas
GENETIC and CHROMOSOMAL DISEASES

FCTI Fetal Precursor Stem Cell Transplants
.... the solution.

Genetic and Chromosomal diseases: Any disorder caused at least partly by defective genes or chromosomes. In humans there are some 4,000 genetic diseases, including cystic fibrosis, Down’s syndrome, haemophilia, Huntington’s Chorea, some forms of albinism, spina bifida, and Tay-Sachs disease. There are four main types of genetic disorders.

Four Main Types of Genetic Disorders

Single-gene genetic disorders
It is estimated that 1 of 200 newborns face a single gene genetic disorder. Some of these are sickle cell anemia, cystic fibrosis, and Huntington disease.

Multifactorial Genetic Diseases
Many well known chronic diseases are Multifactorial Genetic Diseases. These include Alzheimer’s disease, diabetes, obesity, and arthritis. Besides, many cancer types are caused by multiple mutations.

Mitochondrial Genetic Diseases
Mitochondrial DNA is a double-stranded, circular DNA molecule in the mitochondrion. Mutations in the mitochondrion DNA can cause mitochondrial abnormalities.

Chromosomal Genetic Diseases
Down Syndrome is the most well known disease caused by chromosomal abnormalities. In this disorder there is an extra copy of chromosome 21. There are two copies of each chromosome in the cells of healthy humans.

KIDNEY DISEASES

FCTI Fetal Precursor Stem Cell Transplants
.... a different approach.

Kidney Diseases. The kidneys perform a number of functions, chiefly filtering the blood, removing wastes to create urine, adjusting the chemical and fluid balance in the body by controlling the concentration of urine, and participating in the control of blood pressure.

Kidney Disorders

There are three main categories of kidney diseases:

- Acute
- Chronic
- Nephrotic: Diabetic nephropathy, Hemolytic-uremic syndrome, IgA nephropathy, Membranous nephropathy, Acute
LIVER DISEASES

FCTI Fetal Precursor Stem Cell Transplants • treatment of choice

Liver & Disorders

Liver

Hepatitis: Inflammation of the liver, caused mainly by various viruses but also by some toxins, infections or hereditary conditions.

Cirrhosis: The formation of fibrous tissue in the liver, replacing normal liver cells. The death of the liver cells can for example be caused by viral hepatitis, obstruction or contact with other liver toxins chemicals.

Cancer of the liver (primary hepatocellular carcinoma or cholangiocarcinoma and metastatic cancer, usually from other parts of the gastrointestinal tract).

Spinal Cord Injury

The solution...

FCTI Fetal Precursor Stem Cell Transplants + supplementation of EUFs (Eco-ultrafiltrates) of Central Nervous System

Spinal Cord Injury: Spinal cord injury usually begins with a sudden traumatic blow to the spine that fractures or dislocates one or more than one vertebrae. The damage begins at the moment of injury when displaced bone fragments, intervertebral disc, or ligaments bone or tear into spinal cord.

Most injuries to the spinal cord don’t completely sever it. Fractures and compression of the vertebrae predominantly crush and destroy the axons (fibers) of nerve cells. But carry signals up and down the spinal cord between the brain and the rest of the body.

Injury to the spinal cord can damage a few, many, or almost all of these axons. Some injuries will allow almost complete recovery, others will result in complete paralysis.

Data of some of our patients with old spinal cord injuries treated by FCTI Fetal Precursor Stem Cell Transplant in the past:

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Gender</th>
<th>Diagnosis</th>
<th>Location</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35</td>
<td>Female</td>
<td>SCI</td>
<td>L4-L5</td>
<td>Improved</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>Male</td>
<td>SCI</td>
<td>T10-T11</td>
<td>Stable</td>
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<tr>
<td>3</td>
<td>55</td>
<td>Female</td>
<td>SCI</td>
<td>T4-T5</td>
<td>Improved</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>Male</td>
<td>SCI</td>
<td>L3</td>
<td>Stable</td>
</tr>
<tr>
<td>5</td>
<td>75</td>
<td>Female</td>
<td>SCI</td>
<td>L1-L2</td>
<td>Poor</td>
</tr>
</tbody>
</table>

FCTI
FETAL CELL TECHNOLOGIES INTERNATIONAL INC.

The Largest Provider of Fetal Precursor Stem Cells, Autologous Stem Cells & Eco-Ultrafiltrates

www.precursorstemcells.com
Patients consultation with their medical doctor

Doctor make a brief (at least half page) medical summary or fill up the medical standardised questionnaire. Doctors can also attach 1 attachment in "pdf" file or "jpeg" file comprising all relevant medical report if they think are significant importance.

Doctor sent email to:- info@fetal-cells.com

FCTI’s professional team analyze the medical summary and/or medical questionnaire. A prescription of individualised preparation of different type of cells are made if patient is found suitable for Stem Cell Implantation. Doctor would also be informed if respective patient unsuitable for fetal stem cell transplantation.

Doctor consults with patient. A decision is made to take or not to take up the fetal stem cell Implantation. Doctor email to info@fetal-cells.com upon conformation to take up.
6. Full Payment made to FCTI (or Minimum: 50%) at least 17 days before coming scheduled implantation date.

7. FCTI Proprietary Primary Cell Tissue Culture harvesting commence (Time Frame 14 to 17 days preparation)

8. European Human Couriers transport the cells from FCTI Lab/Plant from Vienna to different parts of ASIA in special packaging maintaining the cells in room temperature

9. Implantation of the individualised live fetal precursor stem cells within 24 hours generally and not exceeding 72 hours from time of completion of culturing in our European Plant.

10. Follow up post Stem Cell Implantation report in 3.5 months to 4 months from Doctor to FCTI coordinating team for assessment/data base updating.
For the prevention and treatment of Autoimmune disease, Cancer and etc, please visit http://www.asitherapy.com

For more information on precursor stem cells and proprietary autologous stem cells for treatment of chronic diseases or untreatable diseases, please visit: http://www.precursorstemcells.com

For more information on professional membership and continuing medical education for doctors on stem cells, please contact:
The International Association of Stem Cells Transplantation, USA website at http://www.iasct.org

For other related websites, please log on to:
For more information, please contact:

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THANK YOU