

## 2005 Workshop – Type I

### THE POTENTIAL OF STEM CELLS TO TREAT DISEASE

A Workshop Presentation given by Bryon Petersen Ph.D  
Dept of Pathology for the AGSD(UK) Conference October 2005

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Doctor Petersen began his presentation with the following quotations:

Many a man fails as an original thinker simply because his memory is too good.  
Neitzche

Research is the systematic process of going down alleys to see if they are blind.  
Marston

Definition of a stem cell:

It is generally used to describe a cell that is capable of both self-renewal and differentiation.  
However the term has been used in other contexts.

Types of stem cells:

Embryonic, Fetal, Cord-blood and Adult

Using an adult stem cell would mean that an adult patient could supply the stem cell which would be the best solution "self healing self".

There are many types of stem cells in bone marrow which could be converted to repair damaged parts of the body. It is also thought that the stem cells in the blood, if converted, may be able to repair damage throughout the body as blood exists almost everywhere in the body.

Work began in the 1960's on blood stem cells. However there is still an enormous amount of research to be done and we are only at the tip of the iceberg in this field.

We want to test the hypothesis that stem cells can be used as an efficient vehicle for delivery of a therapeutic genetic material to the liver to correct certain metabolic disorders.

Hallmarks of a successful gene delivery:

1. Targeting the right cells.  
The gene must go to the liver and not the big toe.
2. Activating the gene.  
It must go into the cell's nucleus and be turned on.
3. Integrating the gene into the cells.  
So that it becomes part of the host cell's genetic material.
4. The most important criteria is that no adverse side-effects come from the treatment.  
The treatment must be safe and reliable for the patient

### GENE THERAPY

Gene therapy is the ability to transfer nucleic acid, DNA to treat/correct or prevent a disease.

#### Methods of therapeutic gene delivery

1. Non-Viral such as using cationic liposomes
2. Viral such as using Adenovirus, or Lentiviral vectors

My laboratory is researching the pros and cons of delivering the transgene directly into an organ via a virus or via a stem cell which is derived from the patient.

### CASE HISTORY

An adult female patient with GSD Type I developed Leukemia and was given a bone marrow transplant using bone marrow from a male donor.

After some time the patient was able to stop overnight feeds and could fast for over 9 hours without showing signs of hypoglycaemia.

It became apparent that the donor stem cells had entered her liver and it was able to function normally. Although after two years only one percent was functioning normally she showed no sign of hypoglycaemia as humans only need 10% to 15% of the liver to function and can survive on less.

The liver is an ideal organ for stem cell therapy as not only does it need only a small part of it to function but it also regenerates so that the new normal cells can divide and increase and over take the diseased cells.

In the case of the female patient because the donor was male, staining the X and Y chromosomes distinguished the patient's cells from those derived from the donor.

### CONCLUSION

Our data has indicated that stem cells may play a pivotal role in either the delivery of normal cells to replace damaged native cells or delivering genetic material to organs/patients lacking critical genes.

Our data also indicates that the genetic material could be expressed in the cells with stable integration within the cell's genome on a long-term basis.

Even as advances are being made in the stem cell world extreme caution must still be observed before clinical trials begin.

The ultimate rule that we all must follow is "Do No Harm" in bringing about a cure for patients.

Corollary written for Dr. Wienstien for the AGSD USA newsletter.

The ultimate goal of our research at the University of Florida is to cure Glycogen Storage Disease. The stem cell team, led by Dr. Bryon Petersen and his graduate student Susan Ellor, is currently working on project that will attempt to replace the missing gene in GSD using stem cells to create healthy liver cells. Their work is a fusion between gene therapy and adult stem cell therapy.

Given the right signals, undifferentiated adult stem cells are able to mature into specific cell types including liver cells. In the technique employed at the University of Florida, undifferentiated adult stem cells are removed from the bone marrow of the affected mouse. The corrected gene is then inserted in the laboratory into the adult stem cell using viral gene therapy, and the corrected stem cells are then infused into the blood stream or liver. Dr. Petersen has successfully used this technique to improve biochemical abnormalities in the rat model of another liver disease.

Presently, Dr. Petersen's lab is working in the GSD type Ia mouse model. Once this technique is successful in the mice, it will then be used in the GSD Ia dog model. Stem cell therapy has the advantage of potentially treating multiple tissues, and it may offer the best chance of treating GSD type Ib which involves the bone marrow, liver, and intestines. Future studies are planned in the newly created mouse model of GSD type Ib.