PANCREATIC MULTIPURPOSE PRECURSORS: THE FUTURE OF DIABETES TREATMENT

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Abstract – Derek van der Kooy has recently isolated a cell located in the mouse pancreas termed a “pancreas derived multipotent precursor” (PMP) cell. PMP cells have the ability to differentiate into an insulin producing beta cell. van der Kooy is working toward using PMP cells as a treatment for Type 1 diabetes. He illustrates through a series of experiments that PMP beta cells are insulin-producing cells. Furthermore, these cells are used as a treatment to successfully recover hypoglycemic mice. It can be concluded that PMP cells are a successful treatment for Type 1 diabetes in mice.

1. INTRODUCTION

The human body is home to more than 1013 cells each containing identical sets of deoxyribonucleic acid, or DNA [1]. DNA is the macromolecule responsible for the production of genes and proteins within each cell. It is this variable expression of genes and proteins that allow a cell to become specialized within the body, restricting each cell’s performance to a specific tissue [1]. Despite the importance and necessity of these specialized cells throughout the body, there is a class of cells that remain unspecialized for an indefinite amount of time – stem cells. Derek van der Kooy along with his team at University of Toronto hope to utilize this fascinating characteristic and improve regenerative medicine. What follows is a review of van der Kooy’s findings.

II. TECHNICAL INFORMATION

Stem cells are undifferentiated cells that produce two different daughter cells. One of which is of equal potential and thus has the ability to differentiate, and one of less potential that does not have the ability to differentiate. Thus, these cells are described as being multipotent as they possess the ability to become specialized in a variety of cell types. Current research has identified two classes of stem cells, somatic stem cells and embryonic stem cells. Somatic stem cells can be found in adult tissues throughout the body such as in the brain and bone marrow. Within an organism, somatic cells function to correct damaged tissue and maintain healthy tissue. Unlike somatic stem cells, the development of embryonic stem cells is not limited to a certain tissue within the body. With these novel cell characteristics, the application of stem cells to modern medicine is inevitable. One of the hallmarks of stem cells is their ability to be treated in lab, either with DNA or chemicals to produce a specialized cell type. This remarkable advancement of directed differentiation in stem cells has paved the way for a new field of science called regenerative medicine.

Derek van der Kooy and his team have devoted considerable amounts of time studying stem cells and their regenerative properties in his lab. His most recent work in pancreatic stem cell has allowed him to identify a rare cell located in the pancreas of mice. From this mammalian pancreas, he was able to isolate a “pancreas-derived multipotent precursor” cell, or simply referred to as a PMP cell [2]. What is remarkable about this cell type is its ability to differentiate into two separate cell lineages. The first is of neural lineage and the second is of pancreatic lineage, the latter of which is van der Kooy’s focus [2]. The pancreatic lineage can further differentiate into four cell types. One of the cell types is a beta cell, an insulin-producing cell. The intention of this study is to use beta cells as a therapeutic treatment for diabetes [2].

Diabetes mellitus is a medical condition resulting from the inefficient secretion of insulin from the pancreas. Insulin is necessary for the metabolism of glucose, the main energy source in the body [3]. Beta cells govern the production of insulin [1]. Diabetes exists in two forms, Type 1 and Type 2. Type 1 diabetes, the focus of van der Kooy’s therapeutic work, is the result of the immune system attacking and killing the beta cells in the body. As a result, insulin is produced at inadequate levels [1]. Insufficient production of insulin results in extreme tiredness, blurred vision, weight loss, and frequent infections among other things. Thus, the motivation of van der Kooy’s research is to produce insulin secreting beta cells to be implanted in individuals with Type 1 diabetes.

Recent work has indicated that the pancreas, and thus beta cells are not a result of stem cell differentiation [4]. Rather, the pancreas
is a product of progenitor cells, which unlike stem cells are unipotent [5]. As Stanger et al. (2007) demonstrated, the pancreas is the product of intrinsic factors that produce an organ of pre-determined size, thus eliminating the possibility of stem cell activity [4]. Derek van der Kooy argues that this is simply not the case — somatic stem cells are responsible for the production of beta cells. Through multiple experiments involving the pancreas, van der Kooy proves that the pancreatic stem cells do exist, they exist in the form of PMPs [5]. Furthermore, he illustrates the successful introduction of pancreatic stem cells into a diabetic patient in which symptoms of Type 1 diabetes are alleviated.

The first experiment van der Kooy preformed to support his hypothesis allowed him to prove that PMP cells are a product of the pancreas [2]. Since the PMP cells are a type of stem cell, this would suggest that it is progenitor cells as opposed to stem cells that are acting to develop and maintain the pancreas. The experiment required disproving the proliferation of PMP cells from the neural crest [2]. It is suggested that the neural crest is largely composed of progenitor cells, as opposed to stem [6]. Thus, disproving the emergence of PMP cells as product of the neural plate indirectly suggests the pancreas is not a product of progenitor cells, but is a product of stem cells. In his second experiment, van der Kooy illustrated through multiple assays that PMP cells produce insulin. Upon realizing that the PMP-beta-expressing cells produced a morphology different from adult beta cells, van der Kooy set out to characterize the PMP cells further. He suggested that PMP cells produced insulin mRNA at lower levels compared to adult beta cells [2]. These results allowed van der Kooy to conclude that the low insulin producing PMP cells were a precursor morphology to adult beta cells. As groundbreaking as these findings are, van der Kooy did not stop there. He continued his research with PMP cells to test their efficiency in reversing diabetes in transgenic mice.

For this experiment, van der Kooy utilized both human and mouse PMP cells. Mice were injected with a substance causing diabetes. Of the injected mice, those that exhibited the desired phenotype seven days following the injection were selected. The desired phenotype was hypoglycemic mice, a condition that results from diabetes. The isolated mice were then injected with either mouse or human PMP cells. The experiment was successful as can be concluded from the results indicating reduced hypoglycemia and increased body weight. Furthermore, the results indicated similar restoration of insulin production comparable to a direct transplant of islet cells into the mouse [2]. The ability of PMP cells to rescue a diabetic mouse imply that this method of PMP cell implantation in humans may elicit a similar response, thus proving to be a therapeutic use of stem cells to cure diabetes.

One can predict that the implantation of PMP cells into Type 1 diabetic patients will essentially eliminate most, if not all of the symptoms. The PMP cells will compensate the body’s naturally depleted insulin production. The challenge medical engineers will face is translating these findings into a treatment that does not require invasive surgeries, as this would make it more harmful than beneficial.

III. CONCLUSION

Derek van der Kooy has made extraordinary advancements in the area of stem cell research through his remarkable discoveries. His successful isolation of PMP cells as precursor beta cells is arguably the future of diabetes research and treatment.

IV. REFERENCES


