Meet a Research Group
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The Use of Diabetic Animal Models

The human disease diabetes mellitus has some of the best animal models. This regards type 1 diabetes, also known as insulin-dependent diabetes mellitus or IDDM for which the spontaneously diabetic models of NOD mice and BB rats are highly useful. Also, type 2 diabetes mellitus known as non-insulin dependent diabetes mellitus (NIDDM) has valuable spontaneously diabetic models such as *Ob/Ob* and *db/db* mice. Both diseases are frequent; in Scandinavia 1% of all newborns will develop type 1 diabetes during their lifetime whereas 5% will acquire type 2 diabetes. Therefore, there is an extensive use of the animal models both in context of studying the disease mechanisms with the goal of being able to prevent the diseases, as well as for studying the late diabetic complications. At Bartholin Instituttet we have been interested in type 1 diabetes and during the last decades we have performed studies on BB rats and NOD mice. An example of beneficial use of the animal models is our original study from 1985 on prophylactic insulin treatment of BB rats. These animals develop diabetes between 60 and 120 days of age but when giving insulin daily *s.c.* before and during most of this period we could reduce substantially the diabetes incidence. These results were later confirmed in NOD mice which, in contrast to BB rats, do not need metabolic doses of insulin. Several studies on the mode of action have revealed that both beta-cell rest induced by the insulin treatment, and regulator cells raised against insulin may be active mechanisms. Due to these results several human studies of prophylactic insulin treatment have been performed. The outcome of open studies in USA and Australia show promising effects. In summer 2001 interim results from a large randomised study in USA will be pronounced.

In the last several years we have been interested in sulfatide and other glycolipids which are present in the beta cells and secreted together with insulin. These studies have been performed in collaboration with Professor Pam Fredman, University of Göteborg. Isolated islets of Langerhans have been used in histological and biochemical detection of especially sulfatide and its precursor galactosyl ceramide. Antibodies against sulfatide have been detected both in human patients and in the animal models. Thus, sulfatide is an antigen in the type 1 diabetes disease like insulin and glutamic acid decarboxylase and it is of importance to see whether treatment with sulfatide can reduce the diabetes incidence. In order to do this we used the transfer model of NOD mice in which the result of a given treatment can be obtained within 80 days. Normally, NOD mice develop diabetes later than BB rats and should be followed for 250-300 days. By transferring spleen cells to young NOD mice from newly diabetic mice, the recipient mice will develop diabetes within 20-25 days and the result of a certain preventive treatment can be seen shortly after this period. Here, we have found that treatment with sulfatide or galactosyl ceramide significantly reduced the diabetes incidence. This treatment could well involve raise of NKT cells which are now known to behave as regulator cells. Also, the direct effects of sulfatide on beta cells are studied. These include facilitation of exocytosis of the individual insulin granules and opening of potassium channels.

The diabetic animal models are extensively used all over the scientific world and as the above mentioned examples from our laboratory indicate, these models have been highly valuable in obtaining our present knowledge of the diabetes diseases.

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