Technology Offer

Mutation leading to Type 1 Diabetes mellitus and corresponding animal model

Reference Number 15-00379

Challenge
Diabetes mellitus (DM) represents a group of metabolic diseases with a typical clinical state of hyperglycemia. Type1 diabetes mellitus (T1DM) occurs with an incidence of about 10 % and is less frequent compared to T2DM. Noteworthy, genetic predisposition plays an important role in development of T1DM and therefore T1DM is causative for 90% of childhood diabetic diseases. T1DM is characterized by autoimmune-mediated loss of insulin producing ?-cells and emerging insulin deficiency. A major challenge in studies on T1DM is the low availability of reliable animal models mimicking human pathogenesis. Thus, well characterized animal models are of particular importance in human T1DM related research.

Technology
The herewith presented technology reveals an unknown gene mutation leading to an amino acid exchange in the protein Dock8 (*dedicator of cytokinesis 8*) and a clinical phenotype that closely resembles human T1DM. The mutation was identified in animals of the rat strain LEW.1AR1-*iddm* and it was never described in context with T1DM until its publication in 2014. The *LEW.1AR1-iddm* rat develops insulin-dependent T1DM with remarkable similarities to the human disorder. Results from various *in vivo* studies suggest that these animals serve as an excellent disease model for human T1DM. Remarkably, the amino acid sequence of Dock8 is highly conserved between human and rat. Thus, the recently identified mutation and the corresponding animal model are of particular importance for the elucidation of human T1DM pathogenesis and the future development of therapeutic approaches.

Commercial Opportunity
In-licensing or collaboration for further development is possible.

Development Status
In vitro assays confirmed the mutation in Dock8 and *in vivo* analysis in the LEW.1AR1-iddm rat model proved the relevance of the mutation for emerging T1DM.

Patent Situation
European patent has been granted (EP 2942356; priority of 2014) and validated in DE (602014013382.7), CH, GB, FR.

Further Reading
Arndt T, Wedekind D, Jörns A, Tsiavaliaris G, Cuppen E, Hedrich HJ, Lenzen S. 2015. A novel Dock8 gene mutation confers diabetogenic susceptibility in the LEW.1AR1/Ztm-iddm rat, an animal model of human type 1 diabetes. *Diabetologia*. 58:2800-2809.
Arndt T, Wedekind D, Jörns A, Tsiavaliaris G, Cuppen E, Hedrich HJ, Lenzen S. 2014. Identifizierung der Mutation im Dock8 Gen in der LEW.1AR1-iddm Ratte, einem Tiermodell des humanen Typ 1 Diabetes mellitus. Diabetologie und Stoffwechsel 2014; 9 - FV8 DOI: 10.1055/s-0034-1374865.
Arndt T, Jörns A, Hedrich HJ, Lenzen S, Wedekind D. 2014. Variable immune cell frequencies in peripheral blood of LEW.1AR1-iddm rats over time compared to other congenic LEW strains. Clin Exp Immunol. 177:168-78.
Jörns A, Arndt T, Meyer zu Vilsendorf A, Klempnauer J, Wedekind D, Hedrich HJ, Marselli L, Marchetti P, Harada N, Nakaya Y, Wang GS, Scott FW, Gysemans C, Mathieu C, Lenzen S. 2014. Islet infiltration, cytokine expression and beta cell death in the NOD mouse, BB rat, Komeda rat, LEW.1AR1-iddm rat and humans with type 1 diabetes. Diabetologia. 57:512-21.

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