Development of Novel Antibody-Based Approach for T1D

Manal M. E. Ahmed[1], Walid Nazmy[2], Jakeen Eljakee[3]*

ABSTRACT

BACKGROUND

Type 1 diabetes (T1D) is one of the most common chronic diseases of childhood. It is prompted by the autoimmune destruction of insulin-producing beta cells in pancreatic islets and leaves affected individuals dependent on daily insulin injections. At present T1D treatment is done by lifelong delivery of novel kinds of insulin which have been synthesized recently. Numerous approaches have attempted to prevent or stop islet cell destruction on the basis of immunotherapies to block T cell responses against β cells antigens which are quite common at the time of initiation as well as development of T1D.

OBJECTIVES:

In this study we aimed to develop anti CD3 monoclonal antibodies as immunotherapy to modulate the immune system to get good glycaemic control, to avoid hyperglycaemia as it is correlated with long-term microvascular as well as macrovascular complications along with preventing recurrent hypoglycaemic episodes as they adversely iinfluence cognitive function.

METHODS:

The developed anti CD3 monoclonal antibodies is one of antibody-based approaches which attack CD3/ T cell receptor (TCR) complex, blocking the union of CD3 with TCR and stimulating the development of an anergic state of the T cells. After immunization of 4-week old female NOD mice for 36 weeks, anti CD3 antibodies have shown good efficiency in NOD mice.

RESULTS:

We observed anti CD3 antibodies resulted in the prevention of hyperglycemia, improved glucose tolerance and reduced insulitis. Postponement of C – Peptide reduction in T1D treated NOD mice was stimulated by anti CD3 antibodies. Within a few weeks, anti CD3 antibodies helped preserve C-peptide levels, a byproduct of insulin production that serves as an indirect measure of remaining beta cell function. Immunologic analysis showed that reduction in the pro-inflammatory cytokine IFN-γ and an increase in the anti-inflammatory cytokine IL-10.

CONCLUSION:

We have concluded that anti CD3 antibodies may be an effective therapeutic approach to prevent or delay T1D onset among children and adults at high risk of developing the disease. In the possibility of offering a drug to people who test positive for markers of beta cell autoimmunity but who do not yet have symptoms of disease.

KEYWORDS:

Type 1 diabetes, Monoclonal antibodies, Immunotherapy, CD3, Beta cells

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1- Pharmacology Department, Medical Research Division, National Research Centre, Egypt

2- The holding company of vaccines and biological products, Egypt

3- Microbiology Department, Faculty of Veterinary Medicine, Cairo University, Egypt

**Corresponding Author: thinktankteam2014@gmail.com*