67

Expression of IL – 1β, TGF – β1 and TGF – β1 Receptors Type I, II, III in Salivary Glands of Patients with Sjögren's Syndrome

Diana Mieliauskaite, Irena Dumalakiene, Paulius Venalis, Algirdas Venalis & Zygmunt Mackewicz

State Research Institute of Innovative Medicine, Vilnius, Lithuania

The purpose of this study was to determine the expression of TGF-β1, TGF- β1 receptors (R) type I, II, III and IL-1β in minor salivary glands in patients with primary Sjögren's syndrome (pSS), Sjögren's syndrome secondary to rheumatoid arthritis (sSS + RA) and rheumatoid arthritis (RA). Minor salivary glands biopsy specimens obtained from 20 patients with pSS, 20 patients with sSS+RA and 20 patients with rheumatoid arthritis (RA) were evaluated for TGF-β1, TGF-β1 R I, II, III and IL-1β by immunohistochemistry. Acinar cell IL-1β was decreased in sSS+RA compared with RA. Comparison of the total TGF-β1 showed significant differences between three groups. Significant differences of the total of TGF-β1 R I and R III were found in pSS, sSS+RA and RA. TGF-β1 R II was increased in lymphocytes of patients with pSS. Comparison between the total TGF-β1 and the total IL-1β, and between the total TGF-β1 and the total TGF-β1 R I showed significant differences in all groups. We found significant differences between the total TGF-β1 and the total TGF-β1 R II in pSS and sSS + RA. These results demonstrate misbalance between TGF-β1, TGF- β1 R I, II, III and IL 1β in SS, and may be important in the control of autoimmune epithelitis.

68

Preliminary Characterisation of a Transgenic Mouse with Selective *Igf2* Depletion in the Thymic Epithelium

Marie Mottet, Henri Martens, Chantal Renard, Pierre-Vincent Drion, Olivier Dardenne & Vincent Geenen

University of Liege Center of Immunology, Liege-Sart Tilman, Belgium

The thymus ensures the establishment of central immunological self-tolerance by deletion of self-reactive T cell clones (recessive tolerance) and generation of self-antigen specific natural regulatory T cells (nTreg). During foetal ontogeny, all the genes of the insulin family are transcribed in the thymus according to a precise hierarchy: *Igf2* > *Igf1* > *Ins2* > *Ins1* (1). *Igf2* transcription is defective in the thymus of Bio-Breeding rats, an animal model of human type 1 diabetes (2), and $Igf2^{-/-}$ mice display a lower tolerance to insulin suggesting that thymic IGF-2 could promote significant cross-tolerance to insulin (3).
This study aims at discriminating the respective influences of the central and peripheral arms determining self-tolerance to the insulin protein family. Because of the ubiquitous *Igf2* expression, the selective deletion of this gene in thymic epithelial cells (TEC) should provide important answers to this question. Since FOXN1 is the specific transcription factor for TEC, *Igf2*-loxP and *Foxn1*-Cre mice were crossed in our laboratory.
The presence of the Cre transgene in transgenic TEC and its absence in control TEC was checked by PCR. The weight of transgenic thymus was higher than normal WT thymus, but the general thymic cytoarchitecture was not modified. After selective isolation of TEC, *Igf2* transcripts were markedly depleted in transgenic TEC, and this was confirmed by *in situ* hybridization with *Igf2* probes. Major observation is that glucose transgenic mice aged 4 weeks was significantly higher than that of wild mice (143.3 ± 6.6 mg% versus 112.5 ± 3.7 mg%, $P < 0.005$).
These preliminary data confirm a selective *Igf2* depletion in TEC of transgenic mice. Immunological tolerance to insulin related peptides will be further investigated both in these transgenic and wild type mice.

1 V. Geenen et al. *Curr Opin Pharmacol* 2010;10:461–472.
2 Kecha-Kamoun O. et al. *Diabetes Metab Res Rev* 2001;17:146–152.
3 I. Hansenne et al. *J. Immunol* 2006;176:4651–4657.
(Supported by FRIA and FNRS of Belgium.)

69

Role of the C-Type Lectin-Like Receptor Dcar1 in Oil Induced Arthritis

Britt Nakken[1], Wendi Jensen[1], Peter Szodoray[2], Michael Rory Daws[1] & Sigbjørn Fossum[1]

[1]*Department of Anatomy, Insititute of Basic Medical Sciences, and* [2]*Institute of Immunology, University of Oslo, Oslo, Norway*

We recently mapped a susceptibility locus (*Oia2*) conferring susceptibility to oil induced arthritis (OIA) on rat chromosome 4. *Oia2* was localized to a gene complex containing C-type lectin superfamily receptors (APLEC). Sequence analysis of the APLEC region revealed an early non-sense mutation in dendritic cell immunoactivating receptor 1 (Dcar1) in the OIA-susceptible DA strain, preventing synthesis of the full-length protein. Thus, Dcar1 is a prime candidate for the *Oia2* gene.
We developed a mAb directed towards rat Dcar1 and characterized Dcar1 protein expression on professional APCs in the OIA-resistant APLEC congenic strain. In this strain the APLEC region from the resistant PVG strain has been backcrossed onto the DA strain, conferring