by X-ray crystallographic analyses of FcRn in complex with an IgG derived Fc fragment. Specifically, two conserved histidine residues (His310 and His435) at the C_H2–C_H3 elbow region become protonated at acidic pH and consequently interact with negatively charged amino acids exposed on the α2-domain of the FcRn heavy chain. Genetic fusion of therapeutic proteins to the IgG Fc part takes advantage of the increased half-life of IgG mediated by FcRn. However, preclinical studies indicate that IgG derived Fc fragments have lower half-life than full length IgGs. Based on these facts, we investigated the influence of removal of the IgG Fab arms on Fc binding to FcRn. We will present data that show distinct differences in FcRn binding properties of full length IgG1, an IgG1 derived Fc fragment and Fc fusion variants.

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Comparison of Different Routes of Administration for Influenza Vaccines in a Murine Model

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Influenza is an important respiratory virus and vaccination is the most effective method of prophylaxis. Previous reports have shown that parenteral influenza vaccination induces a rapid systemic immune response, but a poor mucosal immune response. In contrast, an effective mucosal vaccine induces a local immune response, which may block influenza virus at the site of entry and thereby prevent disease and further transmission. Also, a mucosal vaccine can be easily administered without use of needles and can thus be used to protect against future pandemics in the third world countries.

Intranasal vaccination effectively induces mucosal immune responses, but has recently been associated with Bells Palsy (facial nerve dysfunction) and a different mucosal administration route is therefore desirable. One novel route of vaccine administration is application under the tongue (sublingual), but more research is needed to determine how well this route works.

In this study, we therefore compared the local and systemic humoral and cell-mediated immune responses after sublingual, intranasal and intramuscular vaccination. A virosomal H5N1 vaccine, which previously has shown encouraging results for both intranasal and intramuscular administration, was used. We have further evaluated the different administration routes using a promising mucosal adjuvant bis (3′,5′)-cyclic dimeric GMP (c-di-GMP). This is the first report on sublingual vaccination using influenza virosomes and the results are promising.

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Insulin-Like Growth Factor 1 (IGF-1) Promotes Interleukin 7 (IL-7) Synthesis and Secretion by Primary Cultures of Human Thymic Epithelial Cells

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The thymus is responsible for thymopoiesis, i.e. the generation of a diverse and self-tolerant T cell repertoire, including self-antigen specific natural regulatory T cells. Two parameters of thymopoiesis, thymic output of naïve T cells (estimated by sjTREC frequency) and intrathymic proliferation of T cell precursors (estimated by sj/Dß TREC ratio), are severely affected in adult patients with growth hormone (GH) deficiency (AGHD) and GH treatment is able to restore these parameters (1). In AGHD patients, sjTREC frequency is highly correlated to plasma concentrations of insulin-like growth factor (IGF-1), which mediates most of GH actions.

We hypothesized that the thymotropic properties of the somatotrope GH/IGF-1 axis could be relayed by thymic interleukin 7 (IL-7), a cytokine that is essential for V(D)J recombination at the TCR locus and that modulates chromatin accessibility for recombinase-mediated generation of T cell diversity.

Primary cultures of human thymic epithelial cells (TECs) were treated with several doses of recombinant human IGF-1. Supernatants were then recovered and IL-7 concentrations were measured by a highly sensitive ELISA. IL-7 secretion by TECs was significantly increased by IGF-1 in a dose-dependent manner. In addition, the quantity of *IL7* transcripts measured by RT-qPCR in TEC mRNAs was also stimulated by IGF-1. Specificity of these effects was assessed using the IGF-type 1 receptor (IGF-1R)-blocking antibody αIR3. The addition of αIR3 significantly decreased the IL-7 secretion by human TECs stimulated by IGF-1, thus demonstrating the direct involvement of IGF-1R.

These data show that, in humans, thymic IL-7 is clearly implicated in the mediation of the thymotropic properties of the somatotrope GH/IGF-1 axis.

1. Morrhaye G *et al. PLoS One* 2009;**4**:e5668.

(Supported by FNRS of Belgium.)