A SURPRISING AND DRAMATIC NEUROENDOCRINE-IMMUNE PHENOTYPE OF MICE DEFICIENT IN GROWTH HORMONE-RELEASING HORMONE (GHRH)

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In the framework of close interactions between the neuroendocrine and immune systems, Growth Hormone (GH) has been proposed to exert significant effects on the immune response, but there is not yet a general consensus about GH immunomodulatory properties. These studies investigated the development of the immune system and anti-infectious response of dwarf *Ghrh*$^{-/-}$ mice presenting a severe deficiency of the GHRH/GH/IGF-1 axis [1,2].

In basal conditions, different thymic parameters and T-cell responses of *Ghrh*$^{-/-}$ mice were not severely affected but a constant B-cell lymphopenia was observed. We thus decided to investigate vaccine and anti-infectious responses of *Ghrh*$^{-/-}$ mice toward *Streptococcus pneumonia,* a B-dependent pathogen,

Ghrh$^{-/-}$ mice were unable to trigger production of specific IgM and IgG against serotype 1 pneumococcal polysaccharide (PPS) after vaccination with either native PPS (Pnx23) or protein-PPS conjugate (Prev-13) vaccines. These vaccines both include the serotype 1 (our *S.pneumoniae* strain) and provide an effective protection in mice. A short GH supplementation to *Ghrh*$^{-/-}$ mice (1 daily injection of 1 mg/kg GH for 4 weeks) restored the vaccine response to Pnx23 vaccine but not to Prev-13. These data suggest that GH could impact distinct splenic areas. Furthermore, after intranasal instillation of a non-lethal dose (defined by the full clearance by WT C57BL/6 mice after 24h) of serotype 1 *S.pneumoniae*, *Ghrh*$^{-/-}$ mice exhibited a dramatic susceptibility. This was proved by a marked time-dependent increase in pulmonary bacterial, a septicemia already 24h after infection and a survival limit of 72h. We also observed a dramatic decrease in lung B- and T-cell populations and an increase in proportion of inflammatory macrophages. By contrast, WT and heterozygote mice completely cleared *S.pneumoniae* infection after 24h. In conclusion, our data show without ambiguity that the somatotrope GHRH/GH/IGF-1 axis plays an important and unsuspected role in defense against the B-dependent pathogen *S.Pneumoniae*. *Ghrh*$^{-/-}$ mice are currently challenged with other pathogens to assess the specificity of this phenotype.

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