Growth hormone (GH) deficient mice with GHRH gene ablation are severely deficient in vaccine and immune responses against *Streptococcus pneumoniae*

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Abstract

In the general framework of intimate interactions between the neuroendocrine and immune systems, the precise impact of the hypothalamo-somatotrope GHRH/GH/IGF-1 axis upon the immune system is still highly debated. We have previously shown that mice with ablation of growth hormone (GH)-releasing hormone (GHRH) gene (Ghrh⁻/⁻ mice) have normal thymus and T-cell development, but present a marked spleen atrophy and relative B-cell lymphopenia (1-3). Therefore, in this paper we have investigated vaccinal and anti-infectious responses of Ghrh⁻/⁻ mice against *Streptococcus (S) pneumoniae*, a pathogen carrying T-independent antigens. Ghrh⁻/⁻ mice were unable to trigger production of specific IgM after vaccination with either native pneumococcal polysaccharides (PPS, PPV23) or protein-PPS conjugate (PCV13). Human GH (Genotorm) supplementation of Ghrh⁻/⁻ mice partially restored IgM response to PPV23 vaccine but not to PCV13 suggesting that GH could exert a specific impact on the spleen marginal zone that is strongly implicated in T-independent response against pneumococcal polysaccharides.

After administration of a sublethal dose of *S. pneumoniae*, wild type (WT) completely cleared bacteria after 24h, as expected. In marked contrast, Ghrh⁻/⁻ mice exhibited a dramatic susceptibility to *S. pneumoniae* infection with a time-dependent increase in lung bacterial load and a lethal bacteremia already after 24h. Lungs of infected Ghrh⁻/⁻ mice were massively infiltrated by inflammatory macrophages and neutrophils, while lung B cells were markedly decreased. The inflammatory transcripts signature was also significantly elevated in Ghrh⁻/⁻ mice. Important abnormalities of spleen cytoarchitecture and immune cell distribution were observed in Ghrh⁻/⁻ mice both in basal and infected conditions.

This animal model unambiguously demonstrates that the hypothalamo-somatotrope GHRH/GH/IGF1 axis plays a vital and unsuspected role in vaccine and immunological defense against *S. pneumoniae*. In a translational perspective, these data indicate that spleen development and response to anti-pneumococcus vaccines should be cautiously monitored in children with isolated GH deficiency, from congenital and genetic origin in particular.

References

hormone/Growth hormone/Insulin-like growth factor 1 axis of Ghrh−/− mice is associated with an important splenic atrophy and relative B lymphopenia.


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