

Possible intervention of hPGH in the human foetal tolerance through Th1/Th2 balance ?

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Tolerance of the foetal allograft by the maternal immune system in human is a complex multi-factorial mechanism. It has been strongly presumed to involve the CD95/CD95-L apoptotic system, HLA-G, IDO, ILF or the Th1/Th2 balance. This last theory proposes that the shift of the Th1/Th2 balance toward Th2 reduces the inflammatory immune responses and so the probability of foetus rejection. A very interesting question is to know how conceptus could influence this Th1/Th2 balance.

Some years ago, our group has demonstrated the apparition, during pregnancy, of a different growth hormone, the placental growth hormone (hPGH = hGH-V), secreted by placenta and which progressively replaces the pituitary growth hormone (hGH-N). Could this replacement of hGH-N by hPGH exert an effect on the Th1/Th2 balance, and so could this contribute to protect the conceptus against rejection ?

To investigate this possibility, we couldn't perform usual FACS cell-surface marker analysis techniques because, at our knowledge, no discriminating Th1 and Th2 specific membrane protein exists. The only available way was to study the cytokine production pattern. So, beside cytokines's, the mRNAs production tell us about the cellular Th1/Th2 balance status.

We investigated here peripheral blood mononuclear cells, which are the maternal immune cells coming in contact to trophoblastic cells which limit foetal tissues. Blood cells were isolated from women but also from men. Specific mRNA were quantified in a multi-probe RNase Protection assay after short-term cultures.

The results show that :

1. hGHs may act on cytokine mRNAs production.
2. hPGH may act differently as hGH-N.
3. men/women cell responses difference is not higher than inter-individual variations.
4. cells do not seem to respond in a clear Th1/Th2 way ; GHs seem to act differently accordingly to the cytokine considered.
5. high inter-individual variability exists, confirming that peripheral blood mononuclear cells, often describe as mainly quiescent cells, could possess very different immune response capabilities, certainly in correlation with the immune past of the blood donor.

So hPGH appear not to act directly on the Th1/Th2 balance but well on the secretion of given cytokines.