

THYMIC B LYMPHOCYTES – CELLS SECRETING NATURAL ANTIBODIES IN EARLY ONTOGENY

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Natural antibodies that play a role as the first line of defence against a wide spectrum of pathogens were found in the sera of different species during the ontogenical development of the immune system. Minimal amounts of these antibodies were reported to be produced by fetal human B-1 cells, the majority of which express the CD5 molecule.

In this study, pig fetuses, colostrum-deprived newborns and germ-free (GF) piglets (i.e. animals in which B cell development is not influenced by maternal regulatory factors) were used to analyze the occurrence and specificity of natural antibodies. The minute amounts of spontaneously secreted immunoglobulins (Ig) present were assessed with the sensitive ELISA and ELISPOT techniques using isotype specific monoclonal antibodies. Starting at the halfway point in the gestation period, spontaneously Ig-secreting cells (Ig-SC) were detectable in the liver, spleen and thymus. When the total numbers of fetal Ig-SC present were compared, the thymus was identified as the main source of natural antibodies and the only site of IgA and IgG synthesis. In GF animals, the thymus also represented the major site of IgG and IgA production. Substantial augmentation of Ig production by spleen cells was observed in conventionally reared pigs and in G piglets after colonization of their intestine with *E. coli* O86, but no impact of external antigenic stimulation on the number of thymic Ig-SC was found. The antibody repertoire of the first ("preimmune") spontaneously produced Ig was determined using the spectra of the antigens. Antibody against variety of autoantigens (e.g. thyroglobulin, ssDNA, thymocytes), phylogenetically conserved proteins, haptens and bacterial antigens was detected in the sera or in cultured media of cultivated B cells. A flow cytometry analysis of both purified thymic B lymphocytes and peripheral B cells showed that, unlike in humans and mice, in fetal pigs, these cells did not bear the CD5 molecule on their surface, but CD2 was highly expressed in them.

We conclude that thymic B lymphocytes represent the first B cell subpopulation in early fetal ontogeny which is responsible for the production of natural antibodies, not only the IgM, but also the IgG and IgA isotypes. The phenotype of fetal B lymphocytes suggests that they could be compared to human B-1b lymphocytes, i.e. B-1 cells which do not express the CD5 molecule on their surface.