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Antibodies, immunoglobulin genes and the bursa of Fabricius in chicken B cell development

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Abstract

The bursa of Fabricius is critical for the normal development of B lymphocytes in birds. It is productively colonized during embryonic life by a limited number of B cell precursors that have undergone the immunoglobulin gene rearrangements required for expression of cell surface immunoglobulin. Immunoglobulin gene rearrangement occurs in the absence of terminal deoxynucleotidyl transferase and generates minimal antibody diversity. In addition, observations that immunoglobulin heavy and light chain variable gene rearrangement occur at the same time and that allelic exclusion of immunoglobulin expression is regulated at the level of variable region gene rearrangement provide a striking contrast to rodent and primate models of immunoglobulin gene assembly. Following productive colonization of the bursa, developing B cells undergo rapid proliferation and the immunoglobulin V region genes that generate the specificity of the B cell surface immunoglobulin receptor undergo diversification. Immunoglobulin diversity in birds is generated by somatic gene conversion events in which sequences derived from upstream families of pseudogenes replace homologous sequences in unique and functionally rearranged immunoglobulin heavy and light chain variable region genes. This mechanism is distinct from and much more efficient than mechanisms of antibody diversification seen in rodents and primates. While the bursal microenvironment is not required for immunoglobulin gene rearrangement and expression, it is essential for the generation of antibody diversity by gene conversion. Following hatch, gut derived antigens are taken up by the bursa. While bursal development prior to hatch occurs in the absence of exogenous antigen, chicken B cell development after hatch may therefore be influenced by the presence of environmental antigen. This review focuses on the differences between B cell development in the chicken as compared to rodent and primate models.

Keywords: Chicken; Bursa of Fabricius; Antibody; Immunoglobulin genes; Gene conversion; Antibody diversity; Cell surface immunoglobulin; Gut associated lymphoid tissue

1. Introduction

B lymphocytes were first identified in the chicken when neonatal surgical removal of the bursa of Fabricius resulted in birds which failed to make antibodies in response to immunization with *Salmonella typhimurium* type O antigen [1]. Since that time

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it has become clear that the bursa is the primary site of chicken B cell development [2–6] as surgical removal of the bursa during embryonic life can completely prevent the development of B cells and the antibodies they produce. Similarly, it has also become clear that while chickens undergo rearrangement of immunoglobulin gene segments to generate the Ig heavy and light chain V_H and V_L domains, the mechanism by which they generate antibody diversity differs fundamentally from that seen in mouse and human [7–10]. The chicken therefore represents a species in which there has been a co-evolution of lymphoid structure and function away from that seen in the more commonly studied models of rodents and primate bone marrow.

2. Chicken immunoglobulins

Three classes of chicken immunoglobulins have been identified immunochemically [11,12] and genetically [13–15] as homologues to the mammalian IgM, IgA and IgG (Table 1) and their structural properties have been reviewed in more detail elsewhere [16]. Chicken IgM is structurally and functionally homologous to its mammalian counterpart, being present in serum as a high molecular weight pentamer of μ_2L_2 units and being the first antibody generated during a primary antibody response. IgM is also the major class of immunoglobulin expressed on the surface of chicken B lymphocytes.

IgG from a phylogenetic perspective is equidistant from mammalian IgG and IgE and in birds has sometimes been referred to as IgY. Functionally, IgG is generated mainly in secondary antibody responses and behaves like the chicken homologue of mammalian IgG. The designation IgY was originally used for the low molecular weight chicken Ig based on differences in biochemical properties, such as salt precipitation conditions, as opposed to functional characteristics. Given the homology in function between this Ig isoform and mammalian IgG, I would propose using the IgG designation for the chicken isoform. Ducks, unlike chickens however, express two forms of the low molecular weight Ig isoform. One form is full length, analogous to the chicken IgG, the other form is truncated, lacking the third and fourth domains of the heavy chain [17]. I would suggest using the IgY designation for the truncated form since this form shows functional as well as structural differences from the full length IgG [18].

Chicken IgA is found in serum and in secretions such as bile, also similar to its mammalian homologue. There appears to be no chicken homologue to

Table 1
Properties of chicken immunoglobulins

	IgM	IgG	IgA
Molecular mass	~940 kDA	175 kDa	170 kDa in serum 350 kDa in bile 700 kDa in other secretions
Normal serum concentration	1.3 mg/ml	5.0 mg/ml	0.3 mg/ml in serum 2–3 mg/ml in bile
Structure	$\mu_{10}L_{10}$+J chain	γ_2L_2	α_2L_2 in serum α_4L_4+J chain in bile d_8L_8 + J chain in other secretions
Heavy chain structure	70 kDa 5 domains (V_H–Cμ1–4)	67 kDa 5 domains (V_H–Cγ1–4)	65 kDa 5 domains (V_H–Ca1–4)
Homology to human heavy chain	33% to human μ chains	31–32% to human γ and ε chains	35% to human α chains
GenBank accession number (H chain)	X01613	X07174	S40610
Light chain structure	22 kDa 2 domains (V_L–C_L)		
GenBank accession number (L chain)	K00678		