IgT lives! A matter of semantics?

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We read with considerable interest Silverstein's recent Commentary on "Cell-bound antibodies"[1], particularly because it addressed the search for the antigen-specific receptor on T cells that was once a "holy grail" of immunology. Unfortunately, his presentation of the "IgT", or cell-bound Ig, issue sidestepped its membership in the Ig family.

Initial studies showed that the "Igs" detected on the T cell surface differed serologically, biochemically and functionally[2–4] from either secreted serum Igs or those on the surface of B cells. Conventional Igs can be associated with T cells, and many other cell types, as a result of passive adsorption or due to their specificity to self-antigens. However, the central tenet of the "IgT" concept was that the antigen-specific receptor on T cells was a new class of Ig, restricted to the surface of T cells and different from secreted Ig and the cell surface–associated antigen receptors of B cells[5].

Sequence analysis of both the constant domains and the tightly knit variable domains of α, β, γ and δ TCR genes establishes their membership within the Ig subfamily[6], as opposed to the general Ig superfamily, that comprises ~40% of all protein domains. As one testament to their high degree of similarity, antibodies to Ig light chains cross-react with regions of sequence identity in the TCR V_β domain[7]. In addition, PCR probes to shared elements of TCRs and light chains identify both types of transcripts within mammalian systems and in evolutionary comparisons[8,9]. The degree of homology between TCRs and Ig light chains is almost a nuisance: attempts to identify genes specifying TCRs from lower species are routinely foiled due to ready hybridization of probes with genes for Ig light chains.

On the basis of amino acid sequence and genetic organization, the αβ and γδ TCRs are canonical Igs. They arose early in evolution and have been selected to carry out different recognition and functional tasks. The γδ T cells recognize protein and nonpeptide antigens in a manner comparable to that of antibodies, whereas most αβ TCRs are modified to recognize peptide epitopes presented by MHC[10].

The Ig family is rich and diverse[11]. Its members share structural homologies in the framework segments defined by the β strands of the variable as well as the constant domains. These provide the basic structural scaffolding that allows the variable domain loops to impart specificity for protein and peptide epitopes. It is clear that "IgT" does, indeed, exist. Silverstein cogently raises concern about the sociology of science "because each (scientific) advance induces a mindset in the scientist that slants the interpretation of data and new speculations". The fact that the TCR is a new kind of Ig with a direct relationship to "conventional" Igs does not agree with the "mindset" that the TCR is a distinct protein species.

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