High throughput immunoglobulin repertoire analysis of different B cell populations: Clues to the origins of Waldenstrom's Macroglobulinemia

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B cell receptor (BCR) diversity is achieved centrally by rearrangement of Variable, Diversity and Joining genes, and peripherally by somatic hypermutation and class switching of the rearranged genes. Peripheral B cell populations are subject to both negative and positive selection events in the course of their development that have the potential to shape the BCR repertoire. The origin of IgM+IgD+CD27+ (IgM memory) cells is controversial. It has been suggested that they may be a pre-diversified, antigen-independent, population of cells or that they are a population of cells that develop in response to T-independent antigens. Most recently it was suggested that the majority of IgM memory cells are directly related to switched memory cells and are early emigrants from the germinal centre reaction. Advances in sequencing technology have enabled us to undertake large scale *IGH* repertoire analysis of transitional, naïve, IgM memory and switched memory B cell populations. We find that the memory B cell repertoires differ from the transitional and naïve repertoires, and that the IgM memory repertoire is distinct from that of class-switched memory. Thus we conclude that a large proportion of IgM memory cells develop in response to different stimuli than for class-switched memory cell development. Understanding the origins of the different B cell subsets may help elucidate the aetiology of Waldenstrom's Macroglobulinaemia.