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The formation of mutated IgM memory B cells in rat splenic marginal zones is an antigen dependent process

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Previous studies in rodents have indicated that only a minor fraction of the IGHV-Cμ transcripts carries somatic mutations, and is considered memory B cells. This is in marked contrast to humans where nearly all MZ-B cells are mutated. Here we show that the proportion of mutated IgM+ MZ-B cells varies significantly between the various IGHV genes analyzed, ranging from 27% mutated IGHV5 transcripts to 65% mutated IGHV4 transcripts. Excitingly we observed mutated sequences from clonally related B cells with a MZ-B cell and FO-B cell phenotype indicating that mutated IgM^+ MZ-B and FO-B cells have a common origin. To report on the origin of mutated IgM MZ-B cells we have analysed whether rearranged IGHV-Cμ transcripts using IGHV4 and IGHV5 genes from neonatal MZ-B cells and follicular B (FO-B) cells carry mutations. We were not able to detect mutations in any of the IGHV4 and IGHV5 genes expressed by MZ-B cells or FO-B cells from neonatal rat spleen. Since GC's are absent from neonatal rat spleen, these data argue against the notion that MZ-B cells mutate their IGHV genes as part of their developmental program, but are consistent with the notion that mutated rat MZ-B cells require GCs for their generation. Together we conclude that the splenic MZ of rats harbors a significant number of memory type IgM^+ MZ-B cells with mutated immunoglobulin genes and that these memory MZ-B cells are probably generated as a result of an antigen driven immune response in germinal centers.

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