Title
Chance favours the prepared mind.

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and generated mixed bone marrow chimeras, the authors demonstrated that LAG3+CD138+ cells control the expansion of LAG3+CD138+ plasma cells in a LAG3-dependent manner. LAG3+CD138+ cells did not display an amplified response upon re-challenge or undergo isotype switching, indicating that they do not acquire features of B cell-mediated immunity.

Adoptive transfer experiments of different B cell subsets into Rag2−/− mice, as well as cell fate mapping, indicated that LAG3+CD138+ cells can develop from several different B cell subsets and that they have a distinct B cell receptor (BCR) repertoire. Their frequency is strongly reduced in Btk−/− mice, which have defective BCR signalling. In contrast, mice deficient for TLR signalling, CD40 or the Bε T cell receptor, had normal numbers of these cells. This suggests that the development of LAG3+CD138+ cells is BCR-dependent but does not require TLR signalling or T cell help. However, the induction of IL-10 expression was found to be strictly dependent on TLR signalling (except in the bone marrow, where some LAG3+CD138+ cells constitutively expressed IL-10).

Further experiments showed that LAG3+CD138+ cells were also less abundant in mice deficient for CD19, a positive regulator of BCR signalling, and more abundant in mice lacking CD72, which negatively regulates BCR signalling. CD72−/− mice had impaired immunity against salmonella, which could be reversed by treatment with anti-IL-10 or anti-IL-10 receptor.

Together, these results indicate that LAG3+CD138+ cells are natural regulatory plasma cells that rapidly provide a first layer of B cell-mediated immune regulation in response to TLR signals. The authors observed that frequencies of LAG3+CD138+ cells in mice increase with age, leading them to speculate that they may react against antigens released by damaged cells. This may provide a feedback mechanism that senses the number of damaged cells, downregulating immunity accordingly.

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