The importance of resting phases in B cell development

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Everyone preparing for the London Marathon likely knows that to perform their best during the event, they need to rest up now. Research at the Babraham Institute just published in the journal *Science* describes a new mechanism through which B cells ensure that they rest up between intensive developmental events.

Just as our daily routine involves periods of activity, nourishment and rest, the cell cycle describes states that the cell progresses through leading to its division into two daughter cells. Like when we take a holiday, the cell can also pause and take a break after a cell division and this is what researchers call quiescence - a reversible sedentary state.

Researchers at the Institute took a deeper look into how B cells, the immune cells that make antibodies, progress through important developmental stages. In particular they looked at the role of two proteins and how these are able to impose rest periods (quiescence) on cells to ensure that developing B cells 'grow up' properly. The researchers showed that without these rest periods, B cells didn't survive to become functional immune cells. In mice, a 98% reduction of mature B cells was seen when the cells lacked these proteins.

Dr Alison Galloway, first author on the paper and postdoctoral researcher at the Babraham Institute, explained: "We found that the two proteins, RNA binding proteins ZFP36L1 and ZFP36L2, promote cell quiescence by blocking the RNA messages telling the cells to start dividing again. In the same way that we find it hard to function without

sleep, the B cells don't develop as they should if these cell cycle pauses are lost."

Dr Martin Turner, senior author on the paper and Head of the Lymphocyte Signalling and Development research programme at the Institute, commented: "Although roles for transcription factors in establishing quiescence have been established, the contribution of sequence-specific RNA binding proteins was unknown. Our findings shed light on the intricate control and coordination of the cell cycle and show that these binding proteins probably form part of a common mechanism to regulate quiescence, not just one specific to developing B cells."

More information: "RNA-binding proteins ZFP36L1 and ZFP36L2 promote cell quiescence" DOI: 10.1126/science.aad5978

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