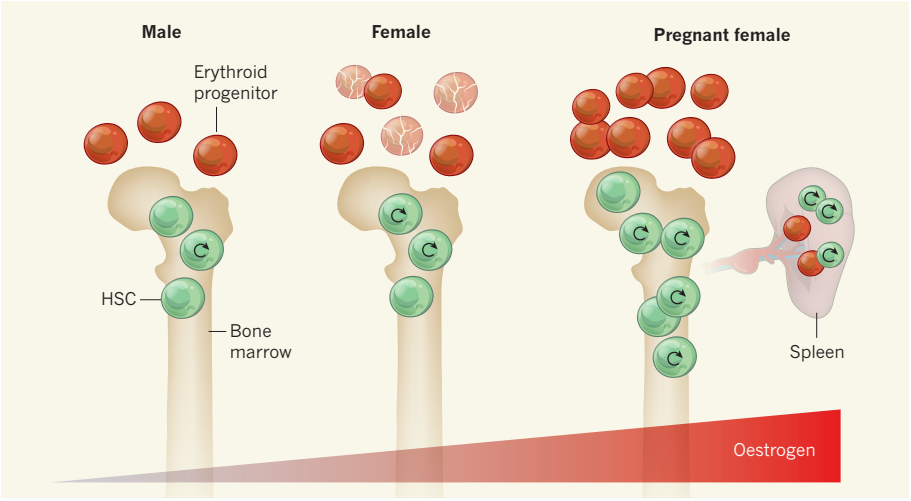

Figure 1 | Oestrogen regulates stem-cell cycling. Nakada *et al.*[5] report that haematopoietic stem cells (HSCs) respond to oestrogen signals, causing female HSCs to divide (circular arrows) more frequently than male HSCs, and produce more erythroid progenitors, which give rise to red blood cells. Despite this difference, the composition of the male and female bone marrow and spleen remains similar under basal conditions, because in females a higher percentage of erythroid progenitors undergo cell death. During pregnancy, however, oestrogen levels increase, leading to an expansion of the HSC population in the bone marrow and spleen, and more erythroid cells in the spleen. This response seems to play a key part in meeting the haematopoietic demands of pregnant females.

predominant oestrogen in females) increased HSC proliferation and drove erythropoiesis in normal and ovariectomized females, as well as in males. Although oestradiol injection was recently reported to induce cell proliferation in a subset of bone-marrow cells[6], Nakada and colleagues' study extends this observation by showing that physiological levels of oestrogen are sufficient to specifically influence HSCs. The authors also show that *Esr1*, the gene encoding oestrogen receptor-α (ERα), is highly expressed in HSCs and is necessary for the enhanced proliferation of female HSCs under steady-state conditions and during pregnancy. Furthermore, they find that oestradiol increases proliferation of wild-type HSCs, but not of *Esr1*-deleted HSCs, strongly suggesting that HSCs respond to oestrogen through ERα.

These findings raise the exciting possibility that the sensing of sex hormones by organs that are not sexually dimorphic may be necessary to orchestrate biological functions such as pregnancy. A key remaining question is whether this oestrogen-induced haematopoietic expansion is necessary for successful pregnancy or for maternal or fetal health. The mechanisms of action and target genes of ERα in HSCs are also not known, and their elucidation will contribute to our understanding of oestrogen-induced HSC proliferation and how it compares with oestrogen-induced responses in other stem cells.

Many genetically modified and naturally occurring mouse strains that have increased HSC proliferation exhibit premature exhaustion of HSC pools[7], so it will be interesting to investigate whether females show more HSC depletion than do males over long periods of time. HSCs are relatively quiescent cells, and this state is thought to protect them from the damage caused by cellular respiration and DNA-replication errors. However, it has also been suggested that DNA repair is more effective in cycling HSCs than in quiescent ones[8,9]. It would be worth testing whether HSCs exhibit sex-specific protection or repair mechanisms that allow female HSCs to sustain increased proliferation. Such exploration could reveal mechanisms by which HSCs might sustain increased proliferation without premature exhaustion or transformation.

Several studies have begun to address the questions of when and how tissue-specific stem cells are mobilized and coordinated by long-range signals in response to the body's systemic needs. Stem-cell function is affected by systemic signals, including those resulting from diet, circadian rhythm, exercise, mating and pregnancy[2]. During pregnancy, for example, increases in oestrogen and progesterone levels coordinate an expansion of mammary stem cells, which is required for remodelling of the mammary gland[3]. And increases in the hormone prolactin stimulate the production of pancreatic β-cells[10] and the proliferation of neural stem cells[4], which may have roles in responding to the increased metabolic load of the pregnant female and in maternal recognition of offspring, respectively. Nakada *et al.* have now introduced the concept that long-range signals act not only in response to specific systemic needs, but also under basal conditions to keep stem cells in a primed state, ready to act when pregnancy is initiated.

Sexual dimorphism in stem cells is understudied, and many stem-cell studies have been performed on only one sex or analysed without distinguishing between sexes. Nakada and

50 Years Ago

Fifty Years of X-ray Diffraction (edited by P. P. Ewald) — The book … provides an extremely refreshing commentary on varieties of organization of scientific research, seen through the eyes of the very young … Wyart coming to Mauguin's laboratory, where there were only two elderly professors, with two elderly servants who kept the place clean and were rather worried about the mess he made, preparing crystals. There is young Schubnikov, trying to buy a lathe to cut crystal sections in Sverdlovsk in 1920 — and, since its price doubled in a few days, spending a million roubles of his own money to get it. There is young Mosley, who could not stop an experiment once he had started it and knew where to get a meal in Manchester at 3 o'clock in the morning … Wars and revolutions necessarily enter into the memories recorded here, though there are only casual references to the adventurous lives led by many crystallographers — to Carl Hermann, for example, working out the crystal structures of the urea adducts in prison … Perhaps most moving is the account of the reunion that took place after the Second World War when Laue himself came to London and met, after a long separation, crystallographers from all over the world. One has, throughout these pages, a very strong impression of being among a very united group of friends — united, as Bijvoet says, by a delight in crystals. **Dorothy Hodgkin**

From *Nature* 25 January 1964

100 Years Ago

The late Capt. Scott's original journals written during his expedition to the south pole, have been placed on view in the manuscript department of the British Museum.

From *Nature* 22 January 1914