

context of the British Isles, it may well make sense in a broader, North Atlantic context. However, as Wright implies, the suggested opening and closing of Iapetus between Laurentia and Baltica may well be the exception in plate tectonic behaviour, and the collision of previously unrelated plates, as exemplified by the British Isles, be the rule.

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## Spleen colony-forming cell as common precursor of tissue mast cells and granulocytes

THE demonstration by Kitamura and his colleagues<sup>1</sup> of the origin of mast cells from CFU-S is persuasive but to us incomplete. Recipient  $W/W^v$  mice with great paucity of mast cells and CFU-S, nevertheless have stem cells which support haematopoiesis and rescue lethally irradiated mice<sup>2,3</sup>. Donated hemi-syngeneic stem cells from single splenic colonies of normal and beige mice must be few, on average of the order of 10 (ref. 4); only a minority of colonies from the tail of the skew distribution have 100 or more which may be necessary to father without mitotic exhaustion<sup>5</sup> a viable population of donated haematopoietic cells so as to compete with the host's established haematopoiesis. Kitamura *et al.* claim 23/106 such occasions (Table 1 of ref. 1); but their Table 2 identifies only 2/106 where erythropoiesis was demonstrable in addition to a raised population of 'mast' cells.

Indeed we question whether mast cells have been demonstrated at all. They used as their criterion cells stained with toluidine blue. The 23 reported cases with whole body distribution are highly biased by cells in spleen. It could be that these are basophil granulocytes of myeloid tissue, possibly but not necessarily equated with tissue mast cells. Note that none of the 106 animals showed mast cells in skin, which is repopulated by donor mast cells when compound  $W$  mice are repopulated with a generous supply of normal stem cells (ref. 6 and our unpublished results).

Others<sup>7</sup> have drawn distinctions not mentioned here between skin and intestinal mast cell populations. Is it not likely that cells staining with toluidine blue are quite heterogeneous and that Kitamura *et al.*<sup>1</sup> are observing the effects

of their procedures on just one or a few of these variants?

Our own unpublished observations indicate that all of a variety of tested  $W$  compound mice lack cells staining with toluidine blue in both skin and intestine. The mice tested include  $W^{sh-2}W^{sh-2}$  (ref. 8), which apart from being black-eyed whites are otherwise substantially normal. Thus the  $W$  locus seems to control 'toluidine-blue-affin' cells as well as pigment migration.

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KITAMURA AND YOKOYAMA  
REPLY—We have reported that the spleen colony-forming cell is a common precursor of tissue mast cells and neutrophil granulocytes<sup>1</sup>. We used mice of two mutant genotypes in the experiment. Giant granules of  $bg^j/bg^j$  mice were used for identification of the origin of both tissue mast cells and neutrophils, and  $W/W^v$  mice were useful recipients because they lack tissue mast cells.

Loutit *et al.* have pointed out a discrepancy between the proportion of mice in which mast cells appeared and that of mice in which donor-type erythropoiesis was demonstrable. As they mentioned,  $W/W^v$  mice have haematopoietic stem cells but their function is apparently abnormal. Numbers of neutrophils, erythrocytes and tissue mast cells in adult  $W/W^v$  mice are respectively ~100, 50 and 1% of the value in congenic  $+/+$  mice<sup>2,3</sup>. The mechanisms which determine such differentiation patterns of abnormal stem cells in  $W/W^v$  mice are unclear. However, the haematological situation in  $W/W^v$  hosts may explain the discrepancy discussed by Loutit *et al.* The transplanted normal stem cells might be selectively committed to tissue mast cells rather than to neutrophils or erythrocytes.

We think that the 'toluidine-blue-affin' cells counted in our experiments are true mast cells for the following reasons. (1) The cells were not only stained with toluidine blue but also contained

histamine and heparin. The histamine concentration in the forestomach<sup>4</sup> and the skin<sup>5</sup> of  $W/W^v$  mice is ~1% the value observed in  $+/+$  mice. Heparin is not demonstrable in the skin of  $W/W^v$  mice<sup>6</sup>. (2) The toluidine-blue-affin cells do not seem to be basophil leukocytes on the basis of their morphology and mode of differentiation. Typical mast cells can be differentiated from typical basophils by morphological criteria<sup>7</sup>. Most toluidine-blue-affin cells which appeared in the spleen of  $W/W^v$  mice after transplantation of spleen colony-forming cells were typical tissue mast cells. Moreover, no typical basophils were detected in smears of the bone marrow, spleen or peripheral blood of mice of any genotypes. Basophils, as well as neutrophils and eosinophils, seem to leave haematopoietic tissues after maturation. In contrast, precursors of our toluidine-blue-affin cells proliferated in connective tissues before final differentiation is characteristic of tissue mast cells<sup>8,9</sup>.

The fact that there was no increase in mast cell number detected in the skin of  $W/W^v$  mice after injection of cells from a single spleen colony<sup>1</sup> may be attributable to the differential demands of mast cell differentiation between tissues. Donor-type mast cells appeared in the caecum and stomach but not in the skin when bone marrow cells of  $bg^j/bg^j$  mice were injected into irradiated  $+/+$  mice<sup>10</sup>. However, the origin of the intestinal mast cells was not different from that of skin because donor-type mast cells also appeared in the skin after local applications of methylcholanthrene to such radiation chimaeras<sup>9</sup>. Moreover, mast cells appeared in the caecum and stomach of 5/9  $W/W^v$  mice but in the skin of only 1/9  $W/W^v$  mice after transplantation of a small number ( $10^4$ ) of bone marrow cells from the  $+/+$  donors<sup>11</sup>, this mouse was also cured of anaemia<sup>11</sup>.

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