ing the last round of cell growth. To examine these possibilities the authors analysed the imaginal discs of the mutants. It turned out that the discs were smaller than usual (as expected) and that the cells in them, which were also small, grew at a slower rate than normal. Thus, in the absence of *dS6K*, a miniature but perfectly formed fly containing the normal number of cells is formed.

In vertebrates the S6 kinases regulate the synthesis of a family of proteins, primarily components of the translational apparatus, in response to the insulin signalling pathway. In S6K1 deficient mice, the derived liver and embryonic cells show unimpaired phosphorylation of S6 thanks to compensation by S6K2 but the gene disruption results in a small mouse. The involvement of protein synthesis in growth control in *Drosophila* is not surprising, a class of mutants called *Minutes* are known to delay development and slow growth rate and division. Also, recently a screen to identify genes required for larval growth identified a translation initiation factor, EiF4A. *Minute* genes encode components of the ribosomal translational machinery. However, these mutations do not alter cell size, showing that cell growth and cell division are normally coupled in order to maintain an appropriate cell size.

This suggests that in the *dS6K* mutant, growth *per se* is not severely impaired; the number of cell divisions required to maintain normal cell numbers still occurs. Thus, dS6K identifies a branch of the insulin signalling pathway likely to be involved in growth control by affecting growth at the cellular level and thereby modulating organ and body size. The challenge now is to find out how this signalling network is controlled in response to environmental and developmental cues. We need to understand what switches it on, and most importantly what switches it off, as this may be the way in which the final body size is determined.

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Should erythrocyte destruction *in vivo* be through phagocytosis alone?

The human body has 3 to 5×10^{13} erythrocytes in circulation. It is estimated that the average life span of an erythrocyte is about 100 days (50 days in rodents) (Bocci 1981; Landaw 1988). About 1% of all erythrocytes (2% in rodents) must therefore be killed each day and in order to sustain the levels of circulating erythrocytes, an equal number must be added daily to the circulation. The processes of erythropoiesis and erythrocyte destruction must be finely balanced to ensure that the required number of erythrocytes stay in circulation, and must be flexible enough to meet contingencies arising due to a sudden loss of blood or an increased demand in oxygen carrying capacity in hypoxic conditions. Erythrocyte numbers can change and remain high (polycythemia) or low (anemia), and this must be

accounted for by altered rates of erythrocyte generation and/or destruction. In order to understand the homeostasis of erythrocytes, the mechanisms involved in their generation and destruction must be clearly understood. While a great deal is known about erythropoiesis and the role played by a variety of cytokines and growth factors in this process (Barosi 1994; Miller *et al* 1994; Jacobsen 1995; Roeder *et al* 1998), the mechanisms involved in destruction of erythrocytes are not well understood. It is believed that aging erythrocytes are trapped in the spleen and bone marrow where phagocytic cells of the reticuloendothelial system remove them (Galili *et al* 1986; Connor *et al* 1994). How aging erythrocytes are recognized by the phagocytes is not clear, though there are several speculations in the literature about the process of senescence of erythrocytes and the changes that may lead to their recognition by the reticuloendothelial system (Hensley *et al* 1989; Kay *et al* 1989; Kosower 1993).

In general, there are two basic mechanisms of removal of unwanted cells in biological systems. These are (i) apoptotic changes or other discernable changes like opsonization of damaged cells, leading to their recognition and phagocytosis by scavenger cells like macrophages, and (ii) direct lysis of cells which can be mediated either by cellular effector elements like cytotoxic T cells and NK cells, or through the activation of the complement system. If cells are killed by a lytic process, internal organelles and debris released by the lysed cells may induce an inflammatory response which may be injurious to the surrounding tissue. On the other hand, if the damaged target cells are phagocytosed, inflammatory responses may be avoided. It should be noted that erythrocytes lack any internal organelles and as such the danger of induction of an inflammatory response following their lysis should be minimal. So far however, the literature lacks specific information about the participation of the lytic pathway in erythrocyte destruction. If phagocytosis is the sole mechanism of erythrocyte destruction, an estimated 2–10 billion circulating monocytes/macrophages along with additional phagocytic cells of the reticuloendothelial system may be involved in phagocytosis of 300–500 billion aged erythrocytes each day. The sheer magnitude of the job of destroying such large numbers of aged erythrocytes makes one wonder why nature would confine all erythrocyte destruction activity to phagocytes and desist from using the lytic pathway to kill aged erythrocytes? It is possible that erythrocyte lysis does take place but has escaped notice since its demonstration is relatively difficult. If erythrocytes are co-cultured with immunocytes, there would be morphological evidence for phagocytosed erythrocytes in the form of internalized erythrocytes. Lysed erythrocytes on the other hand would simply vanish from the culture leaving no trace. Lack of published evidence for lysis of erythrocytes could thus be due to the fact that phagocytosis is easily discernable whereas lysis is not.

We have explored this issue recently and have presented evidence indicating that murine erythrocytes are lysed efficiently by immunocytes *in vitro* (Saxena and Chandrasekhar 2000). We observed that the number of erythrocytes decline progressively if cultured in the presence of leukocyte preparations derived from murine spleen, bone marrow and thymus. The decline was not entirely due to phagocytic activity because depletion of phagocytic cells did not abolish the erythrocyte depleting activity (EDA) of leukocyte preparations. In addition, fixing of effector leukocyte preparations by araformaldehyde treatment did not lower their EDA, strongly suggesting the involvement of non-phagocytic mechanisms in erythrocyte destruction. Assessment of erythrocyte lysis by the chromium release assay of cytotoxicity also provided direct evidence of erythrocyte lysis by leukocytes. T cells appear to be indirectly involved in EDA associated with leukocyte preparations because spleen cells from athymic nude mice were devoid of erythrolytic activity and EDA of normal mouse spleen cells was boosted by the T cell mitogen Con-A. Finally, we provided evidence for the participation of Fas–FasL and TNF–TNFR interactions in cell mediated lysis of erythrocytes. These results indicating that besides phagocytosis, direct lysis of erythrocytes is possible, may have far-reaching implications. Since the homeostasis of erythrocytes in blood circulation is crucial for sustaining life, factors which participate in erythrocyte homeostasis should be clearly defined and their regulation understood. A novel lytic pathway for erythrocyte destruction should focus attention on gaining understanding of the extent to which this pathway contributes to actual destruction of erythrocytes *in vivo*, and the factors which regulate this pathway of erythrocyte destruction. We have no information at present regarding whether, and to what extent, direct lysis of erythrocytes contributes to the turnover of erythrocytes *in vivo*. While there are methods available to study the overall turnover of erythrocytes *in vivo*, appropriate experimental approaches need to be developed to estimate the relative importance of different

possible pathways in the whole animal. We are at present trying to adapt the chromium release assay of cytotoxicity for this purpose.

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Transfer of learning across the somatosensory cortex

It has long been known that the somatosensory cortex in the human brain contains a ‘map’ of the human body. The map is made up of columns of cortical tissue within which the cells respond best to stimulation of ‘their’ designated body part. Such body maps have been seen in virtually all animals that have been studied. The maps have been shown in some cases to be dynamic, in the sense that experience can alter their precise structure. It appears that the brain at birth is given a particular map, which it then adjusts according to what it experiences in its lifetime.

If this is true one can ask, Do neighbouring regions of the cortex share their information? To address this question, Justin Harris at the University of New South Wales, Australia and Mathew Diamond and Rasmus Petersen at the International School of Advanced Studies, Trieste, Italy, decided to utilize the well-studied rat whisker system. The rat’s whiskers are arranged on the side of its snout in a neat five by seven matrix. Correspondingly there is five by seven matrix of cortical tissue columns in the somatosensory region of the rat’s cortex.

The rats were firstly trained in the Gap Cross Task. This task required rats placed in the dark on a plat-