answer this question we followed the route of caveolae/caveolin-1 in HepG2 cells by immunocytochemistry on ultrathin frozen sections and Western blot analysis of purified membrane fractions under the inductive effect of albumin.

We found that the number of caveolae at the plasma membrane strongly depended on the presence of albumin. As it was expected albumin induced the internalization of caveolae. To study whether caveolar endocytotic machinery can join to the classical endocytotic pathway, late endosomes/lysosomes and caveolae were labeled with anti-CD63 (LIMP-1), and anti-caveolin-1 antibodies on ultrathin frozen sections respectively. Long term (1 and 3 hours) albumin treatment resulted in the appearance of albumin containing caveolae in special multicaveolar complexes and caveosome-like structures. Numerous late endosomes/multivesicular bodies were characterized by CD63 (LIMP-1) contained caveolin-1 suggesting that caveolin-1 entered the degradative pathway. Our Western blot analysis showed that albumin uptake resulted in a significant decrease of caveolin-1 in the cytoplasmic membranes (including late endosomes and lysosomes) providing further evidence about the degradation of caveolin-1. Inhibition of the endosomal and lysosomal fusion by monensin has not changed the level of caveolin-1 present in the cytoplasmic membranes. Cycloheximide treatment blocked the appearance of caveolin-1 on the plasma membrane indicating that protein synthesis is necessary for new caveolae formation.

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The adaptability, flexibility and versatility of haematopoietic stem cells

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Stem cell populations are not characterized by the possession of distinctive morphological features but can be defined operationally using their ability to maintain self-renewal while providing an appropriate output of precursors to one or more maturation compartments. They must therefore be capable of generating new stem cells and strictly speaking a transplanted stem cell population should be capable of restoring a depleted population in a primary recipient and subsequently in a secondary recipient. The immediate progeny of stem cells are termed "progenitor cells", which provide an appropriate output of precursors to one or more lineages. Progenitor cells lose the ability to maintain self-renewal but are distinguished by their enormous clonogenic capacity. The ability of a stem cell population to respond to variable demands thus depends upon the susceptibility of its progenitor cell output to regulatory mechanisms. This is correctly termed "stem cell plasticity", a term frequently used to designate the versatility of self-maintaining cell populations, although It does not differentiate between their versatility, flexibility and adaptability. The adaptability of a stem cell population can be defined as the ability to adjust its output of precursors to a single maturation compartment, which can for instance enable the rate of proerythroblast production to be increased in response to hypoxia. Adaptability can usefully be distinguished from flexibility, the ability of a multipotent stem cell population to regulate the distribution of such adjustments between two or more maturation compartments and versatility, the ability of a stem cell population to contribute to the production of previously unexpected progeny. The concept of stem cell versatility has been generated during the past decade or so by the demonstration of donor specific markers and the concurrent expression of cell specific markers in transplanted bone marrow-derived cells, which appear to have been assimilated into several populations of host cells derived from each of the three germ layers. The initial contention that versatility can be attributed to the trans-differentiation of transplanted cells has subsequently been endorsed. The use of host specific markers, in addition to donor specific markers and cell specific markers, has however revealed the formation of hepatocytes, skeletal muscle fibres and neurons in which heterokaria that have derived markers from both the donated cells and the cells of the host reflect the fusion of donor cells with host cells. It has thus become evident that while versatility may depend upon trans-differentiation, apparent versatility may result from cell fusion. These alternatives may both be important during development and regeneration as well as in cell replacement therapy. In some instances the replacement of damaged host cells by donor cells, with or without trans-differentiation, may be the only available option but in others the modification of viable but imperfect host cells by fusion with donor cells may be infinitely preferable. Thus following the destruction of irradiated blood cell precursors replacement is essential, whereas the modification of liver cells deficient in a single enzyme is a far more elegant alternative, if the polyploid heterokaria and the reprogrammed genes generated following fusion are not

potentially dangerous. In interpreting apparent versatility it remains important to recognize that in some instances it may be due to the heterogeneity of donor cell populations. While precise information is being accumulated about stem cell plasticity, attempts to develop stem cell replacement therapy will no doubt continue and include attempts to use bone marrow derived cells to replace or modify deficient or defective cells in the myocardium, the liver, the nervous system and elsewhere as well as in the bone marrow itself. These attempts can reasonably be encouraged - provided that their use is carefully monitored and rigorously evaluated.

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Layer V/VI spiny inverted neurons

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In this paper, we present an account of past and current research being carried out on spiny inverted neurons — alternatively also known as "inverted pyramidal neurons" — in rats, rabbits and cats. In our laboratory, we have studied these cells with a battery of techniques suited for light and electron microscopy, including Nissl-staining, Golgi-impregnation, dye intracellular-filling and axon retrograde-track-tracing. Our results show that spiny inverted neurons make up less than 8.5% and 5.5% of all cortical neurons in the primary and secondary rabbit visual cortex, respectively. Infragranular spiny inverted neurons constitute 15% and 8.5% of infragranular neurons in the said animal and areas. Spiny inverted neurons congregate at layers V-VI in all studied species.

Studies have also revealed that spiny inverted neurons are excitatory neurons which furnish axons for all sorts of cortico-cortical, cortico-claustral and cortico-striatal projections, but not for non-telencephalic centres such as the lateral and medial geniculate nuclei, the colliculi or the pons. As a group, each subset of inverted cells contributing to a given projection is located below the pyramidal neurons whose axons furnish the same centre. Spiny inverted neurons are particularly conspicuous as a source of the backward cortico-cortical projection to primary visual cortex and from this to the claustrum. Indeed, they constitute up to 82% of the infragranular cells that furnish these projections.

Spiny inverted neurons may be classified into three subtypes according to the point of origin of the axon on the cell: the somatic basal pole which faces the cortical outer surface, the somatic flank and the reverse apical dendrite. As seen with electron microscopy, the axon initial segments of these subtypes are distinct from one another, not only in length and thickness, but also in the number of received synaptic boutons.

All of these anatomical features together may support a synaptic-input integration which is peculiar to spiny inverted neurons. In this way, two differently qualified streams of axonal output may coexist in a projection which arises from a particular infragranular point within a given cortical area; one stream would be furnished by the typical pyramidal neurons, whereas spiny inverted neurons would constitute the other source of distinct information flow.

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