IN THE NEWS

Welcome to the genus? A long-standing debate was reignited this month by Morris Goodman and colleagues at the Wayne State University in Detroit, who claim that humans and chimpanzees "are so alike at the level of their DNA that they should both be classified as members of the human genus *Homo*" (*The Independent*).

This controversial idea is not new. In 1991, Jared Diamond at the University of California dubbed humans "the third chimpanzee" and last year, Simon Easteal at the Australian National University agreed that this "makes sense; they are very similar to us, in genetic terms" (*The Age*).

Previous estimates of the genetic similarity between humans and chimpanzees have ranged from 95–98.5%, but Goodman's figure of 99.4%, based on functional sequences, is the highest yet.

The new analysis also indicates that the two lineages split only 5–6 million years ago, which Goodman believes is strong support for his case and "should dictate whether they belong within the same genus" (*New Scientist*).

Criticism of this research — "the figure that you get depends on precisely which genetic differences you look at" (*BBC News*) — has been welcomed by Goodman, who hopes that the discussion will prompt a symposium to "determine if this is a reasonable proposal" (*USA Today*).

But "would it make a real difference if chimpanzees were members of the genus *Homo* rather than *Pan*?" (*The Guardian*). It would seem so, as the ethical and legal implications range from "the use of chimps in laboratory experiments … (to) their conservation in the wild" (*New Scientist*) — with this issue "a small change in classification translates into a big one in moral attitudes" (*The Guardian*).

Victoria Kitchener

CANCER GENETICS

A wake-up call

According to the classic model for cancer progression, cells incrementally acquire genetic and epigenetic changes that lead to fate transformation; further genomic events initiate tumour invasiveness and subsequent metastasis. But reports that expression of some genes in the original tumour can be indicative of the future development of distant metastasis cast a shadow of doubt on this model. Given some clinical features of cancers, notably the fact that secondary tumours can be detected in the absence of an obvious primary tumour, the classical model has become rather shaky. Schmidt-Kittler *et al.* add another blow to the old theory by showing that breast cancer cells metastasize earlier than expected, having accumulated fewer genetic abnormalities than had previously been thought. With important diagnostic and therapeutic implications, the authors propose that the metastatic characteristics are acquired after the cells have left the site of the primary tumour.

Wanting to understand the nature and dynamics of genetic changes that underlie systemic cancer progression the authors studied breast cancer cells from the primary tumour and the progenitors of later metastasis. For breast cancer, the bone marrow is the best source of the latter. Because it has been well documented that epithelial-specific cytokeratin (CK) positive cells in bone marrow are a strong predictor of skeletal metastasis and overall survival, the authors focused on this cell type. They used single-cell comparative genomic hybridization (CGH) to perform comprehensive genomic analysis of these cells.

CGH revealed differences in genomic aberrations between CK cells from patients with and without metastasis. Comparing the CK cells with the primary tumours from which they had originated clearly showed that genetic aberrations in CK cells were different from those in primary tumour cells, suggesting that abnormalities accumulate independently in the two cell populations. Schmidt-Kittler and colleagues also saw that CK cells carried fewer abnormalities, and lacked signs of telomeric instability as long as clinically detectable metastasis was absent. All this indicated that these cells must leave the primary tumour much earlier than was previously anticipated.

So, the authors convincingly showed that it is time to discard the old model of cancer progression — but they didn't end there. For each single-cell genome they also calculated a predictive value for the absence or presence of clinical metastasis. When they tested the predictive powers of a single-cell genotype on cells from patients, the success of correct diagnosis was as much as 85%, providing a way to identify the clinical status of patients from single-cell genome analysis.

As well as scientific and diagnostic value, this study has an important message for cancer therapy. Because of genetic differences between disseminated cells and primary tumour cells, strategies that target cells with advanced genetic changes in primary tumours are unlikely to eradicate the cells that have already left the primary tumour and might later become seeds of metastatic growth. After this wake-up call, the hunt for therapeutic approaches that target disseminated cancer cells is likely to begin.

Magdalena Skipper

References and links

ORIGINAL RESEARCH PAPER Schmidt-Kittler, O. *et al.* From latent disseminated cells to overt metastasis: genetic analysis of systemic breast cancer progression. *Proc. Natl Acad. Sci.* (10.1073/1331931100)