Chromosome 6

by Robin Cook

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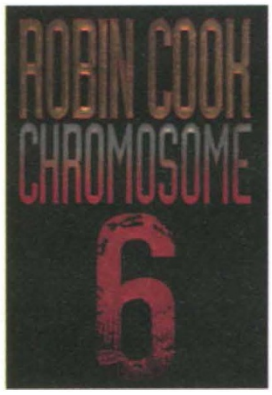
At first I was surprised when asked to review the thriller *Chromosome 6*, by Robin Cook, but after reading the first few pages, I understood. With *Chromosome 6*, Cook, a writer of very popular fiction, is on the trail of a controversial and cutting edge technology — xenotransplantation.

In the real world, xenotransplantation is undergoing intense public scrutiny of difficult and complex issues. Fiction, however, has the luxury of painting with broad strokes and making the issues satisfyingly clear — there are good guys and bad guys. In Cook's case, he has pitted re-occurring characters, Jack Stapleton, the prodigious forensic pathologist, his on-and-off again girlfriend and fellow pathologist, Laurie Montgomery, and a cadre of do-gooders, against the dark side: those misguided greedy M.D.s and a biotech company that supports their research. To remove all doubt, he has even thrown in the Mafia. So the good guys are on the trail of these morally bankrupt clinicians before they do more harm. The plausibility factor is presented under the guise of financial belt tightening in today's medical marketplace; clinicians agreeing to identify rich clients who just might need an organ transplant, to buffer their income which has taken a hit from managed health care. Even if that weren't compelling enough for riveting fiction, we have Kevin Marshall, a stellar but nerdy molecular biologist who has been wooed away from academia with the promise of being given great labs and infinite support to pursue his new research interest, making transgenic chimps. As it turns out Kevin's conscience eats away at his ego-driven attempts to create even better transgenics and he and two fellow animal technicians begin to see the negative impact of this research on the development of these chimeric protohumans, as he calls them.

The plot involves the development of transgenic bonobo chimps, fashioned to provide selected patients with custom made replacement parts. The chimps are engineered to express a full complement of human MHC (major histocompatibility complex) genes taken from their prospective recipient clients, and since these human genes are expressed on all tissues, a perfect donor-recipient match is guaranteed. Certainly the plot is palpable, but in reality one or two technological "refinements" must be awaited! For example, MHC genes are distributed across a fairly large area of the short arm of chromosome 6, demanding that one introduce a huge chromosomal fragment such that appropriate rearrangements can occur. Interestingly, while this seems like pure science fiction (and the author simply invokes a new technologic breakthrough — transposonases — to accomplish it), recent studies with mice make this scenario feasible. Large human artificial chromosomes (HACs) can be successfully introduced into mice resulting in the stable expression of high levels of human immunoglobulin in a tissue specific manner. So, introducing a chromosomal fragment into chimps is not so farfetched as it seems at first.



Perhaps it is because the overall fiction of this tale of science and morals is not entirely foreign, that I found Cook's basic premise of producing chimps with human MHC, a powerful and strange setting to debate animal transplants. Cook brings together many of the issues being debated today in xenotransplantation and unlike the current climate in scientific research, he takes on the difficult task of asking about the ethics of making altered animal forms to suit human needs. Again, by exaggerating those changes — the chimps walk and even have a language — Cook forces the reader to ask ethical questions. Should we be dumping human genes into a highly intelligent species simply to produce replacement organs in humans? Most scientists would cringe at the thought of using chimps in this way but what about baboons? Is there really anything wrong with the idea of the provate corporate development of such technologies, to be used by a very few rich individuals? Perhaps Cook needed to invoke the Mafia to force the reader to see these experiments in a truly negative light. If instead, the scientists were creating chimeric baboons to tackle childhood leukemia, rather than pointing a finger, would we be marveling at the prospect of a brilliant medical breakthrough?

Particularly disappointing was Cook's failure to stir into his plot the possibility of transmitting infectious diseases along with his xenografts — surely the most compelling reason to hesitate over xenotransplantation — and given that many of Cook's previous books have an infectious disease element, this failure was all the more baffling. By introducing large chunks of human genetic information without knowing what those chunks contain, could clearly provide the potential for recombination between human and chimp viruses — a literary opportunity missed. I was also amazed that Cook chose to place these transgenic chimps on an island where they were allowed to roam freely. Indeed, Colobus monkeys became a bonobo delicacy leading me to wonder what viruses might have been conferred by such entrées. The plot also calls for the liberation of 40-odd chimps and whereas this may make for good fiction, it would present a public health nightmare. On the other hand the major behavioral changes seen in Cook's chimps — hunting, building fires, and the like — was amusing, not to mention, hopelessly unlikely given that all these behaviors were presumably carried over with the cloned chunk of human chromosome 6. And why should we assume that such changes would funnel these protohumans in the direction of human evolution rather than some hitherto unknown evolutionary path that may have greater adaptive value?

Although the assumption that there is a clearly visible line in the sand between the good and evil of xenotransplantation, makes for good reading, in the real world the two sides of the debate are not so easily distinguishable and there are no easy decisions to be made on how best to proceed with these new technologies. If only life were that simple.

Scientists and transplant surgeons are in the midst of trying to relieve suffering by developing a new technology involving animal organs, while at the same time facing a need to protect public health such that we don't create more suffering in the long term. As far as I can tell, the only Mafia in the real debate over xenotransplantation is represented by infectious diseases and uncertainty.