MGH Pediatric Orthopaedic Research: Applied Biosurgery

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A Massachusetts biotechnology corporation has recently combined several of its endeavors under a single entity entitled "Biosurgery." Its mission is to bring biotechnology to surgery. Biotechnology is already present in medicine with the application of polypeptide messengers and enzymes in replacement therapy. Surgery frequently requires tissues or organs and has been a more demanding arena for the application of the products of biotechnology to date. Further, by comparison, prosthetics for reconstruction of the mature skeleton provide excellent solutions.

It may be a propitious time to consider the role of pediatric orthopaedics within the entire field of orthopaedics in the context of biosurgery. Pediatric orthopaedics has always been important within our training programs. The prime imperative is, of course, taking care of our young. However, beyond this is the tremendous perspective gained from caring for the skeleton at various stages of development. It really is applied biosurgery. One need only consider techniques such as distraction osteogenesis or the markedly different healing response of osteochondritis dissecans in childhood versus adolescence to think what might be accomplished with renewed stem cell populations, messengers and matrices in the mature skeleton.

The pediatric orthopaedic unit within the Orthopaedic Department of the MGH has a long-term commitment to meeting this challenge: giving the highest quality clinical care and researching areas that would help children and advance the entire field of orthopaedics. The pediatric orthopaedic unit has as its major research goal the development of an autogeneic biological joint that grows. This would be of great benefit for children with congenital limb differences such as proximal femoral focal deficiency (PFFD). Spin-offs of such a technology might have more immediate and wider demographic application such as in the reconstruction of focal articular cartilage defects in the mature skeleton.

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The following is a brief review of what has been accomplished to date and where the research efforts of the MGH pediatric orthopaedic unit is heading. The replantation of an autogeneic growing joint was reported twenty years ago.[1] Unreported research with allogeneic growing joints indicated vascularized allogeneic transplantation of growing tissue would be an extremely difficult problem. As an aside, our experience with allogeneic vascularized composite tissues makes us strong supporters of Dr. Herndon's editorial position.[2] This led us to conduct transplantation experiments with syngeneic mice. It enabled proof of principle that developing joints could be transplanted into a host organism of identical genetic composition in a murine model.[3] This is biosurgery at the level of a small animal model.

The obvious problem in extending this to a non-inbred species such as *Homo sapiens* is the lack of autogeneic tissue. The research endeavors of the unit have branched out at this point to include tissue engineering and developmental biology. Some preliminary work gave support to the hypothesis that a developing joint from one species could be devitalized and serve as the scaffold for seeding with cells from another species.[4] Were this technology perfected, it might be applied to a neonate with PFFD as follows. A developing hip joint from a pig could be devitalized and seeded with cells obtained and expanded from the iliac apophysis of the affected neonate. Various messages might have to be applied to this tissue-engineered construct to recapitulate some of the developmental processes needed for cytodifferentiation.[5] The biological joint thus made could be surgically transplanted to the hip region in the neonate with the only viable chondrocytes being autogeneic.

We are presently engaged in NIH-funded research with Dr. Julie Glowacki to make a biological joint. We have developed improved methods for seeding viable chondrocytes onto a devitalized developing joint.[6] We will be reporting experience with the whole joint construct later this year.

One of the spin-offs of this work has been technology for side-to-side bonding of cartilage.[7-9] We are applying this biosurgery to meniscal repair. In collaboration with the Sports Medicine Unit, Dr. Thomas Gill, CIMIT and the MGH Plastic Surgery Service, we are working with a large animal model for clinical application.

Pediatric orthopaedics and pediatric orthopaedic research are alive and well at the Massachusetts General Hospital. We look forward to working with our colleagues within our Department, our Residency Program and around the world.[10]

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