Department of Plastic and Reconstructive Surgery

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General Summary

Research in the Department of Plastic and Reconstructive Surgery is focused on 4 basic areas: 1) the etiology and treatment of craniofacial anomalies, 2) the etiology and treatment of hand and foot anomalies, 3) the mechanism of wound healing and the grafting of skin and bone, and 4) microsurgical transplantation. The faculty of the department consists of surgeons representing virtually all areas of plastic surgery and clinicians from related disciplines. This diversity provides a stimulating atmosphere necessary for productive research. The participation of plastic surgery residents and postresidency fellows in research studies provides important experience and expands their understanding of anatomical and physiological factors involved in these special areas of surgery.

Research Activities

Gene analysis and staged surgical procedures in patients with syndromic craniosynostosis

Apert syndrome, or acrocephalosyndactyly I, is an autosomal dominant disease caused by allelic mutations of fibroblast growth factor receptor 2 (FGFR2). Two regions (Ser 252 Trp and Pro 253 Arg) of the FGFR2 gene are believed to be responsible for syndromic craniosynostosis. Four monoclonal antibodies that respond only to the peptides derived from mice with a mutation of Pro 253 Arg have been successfully prepared.

Gene transfer into limb bud using electroporation technique

Electroporation was used to transfer genes into the extremities of cultured mammalian embryos. Ell Std-ddy mice were anesthetized with ether. Embryos, together with the placenta and embryonic membranes, were dissected from the surrounding decidua. The yolk sac, amnion, and chorioallantoic placenta were preserved in Hank's Balanced solution. An injection of 0.1 μl of pEGFP-N1 vector was made into the yolk sac. The extremity was grasped with forceps-type electrodes and electroporated with 3 pulses of 30 to 50 V for 50 microseconds. After the amnion had been removed, the embryo was placed in a bottle filled with mouse serum solution. Ninety-five percent O_2 and 5% NO_2 were supplied to the bottle via a tube 4 times a day. The embryo was cultured at 37°C and rotated 30 times per minute for 24 hours. The placenta was removed, and the embryo was fixed in 4% paraformaldehyde. With liquid nitrogen, frozen sections were prepared and observed with fluorescent microscopy. With 50-V pulses, green fluores-

cent protein was observed throughout the entire embryo but was observed in a more restricted area with 40-V and 30-V pulses. In embryos electroporated with 30-V pulses gene transfer was localized to the epidermis and dermis.

Distraction osteogenesis

The use of distraction osteogenesis in reconstruction continues to expand and evolve. Studies of the effects of the various rates and frequencies of distraction have shown that a rate of 1 to 2 mm per day is adequate for the craniofacial skeleton. Dividing daily distractions into smaller, more-frequent distractions accelerates bone formation. We have developed a device with a built-in motor that can produce continuous distraction. Results of experiments using newly developed devices are being analyzed.

Morphologic study of bone conduction mechanisms

Experiments of artificial bone osteoconductivity have involved the extremities more often than the cranium. For this reason we performed an experimental study of osteoconductivity of β-tricalcium phosphate (β-TCP) in a cranial bone defect. Bone regeneration was evaluated in full-thickness circular defects (10 mm in diameter) created bilaterally in the parietal bones of adult female Japanese white rabbits. The rabbits were divided into 3 groups. In group A, a 9.5-mm-diameter, 2.0-mm-thick β-TCP disk was inserted into the bone defect. In group B, a 0.1-g granule of β-TCP was inserted. In group C, nothing was inserted. The periosteum was repaired, and care was taken to avoid damage to the dura. Bone regeneration was assessed with macroscopic examination, roentgenometry, strength, and histological examination. The results show that β-TCP has good biocompatibility with cranial bone.

Tissue engineering

Flaps lined with mucosa are in great demand for nasal, oral, tracheal, and urogenital reconstruction. Fascia lined by mucosal tissue has been developed as a new reconstructive material. Sublingual mucosa was obtained from Japanese white rabbits, and separated mucosal cells were subcultured twice for 4 weeks. The cells were transplanted to the fascia of the femoral muscles in the same rabbits. The fascial tissue was removed with the muscular tissue 1 week after transplantation. The specimens were stained with hematoxylin and eosin, and immunohistochemical staining for cytokeratin, a specific marker of mucosal cells, was performed. The growth of mucosal tissue was confirmed histologically. Fasciomucosal complex tissue had developed. Fascia proved to be a useful scaffold that cross-links between the transplanted mucosa and the muscle.

Hemodynamic analysis of capillary blood vessels in diabetic patients

The increased prevalence of diabetes has increased the prevalence of diabetic foot gangrene. Below-knee or above-knee amputation should be avoided for as long as possible by using both conservative and surgical treatment. However, few effective methods that can be used to predict diabetic foot lesion have been reported except for the ankle-arm pressure index and the cardio-ankle vascular index. We found that video-microscopic hemodynamic analysis of blood flow through capillary vessels in the

pedal eponychium in patients with diabetes can indicate the stage of microangiopathy and may predict diabetic foot lesions. This new device will be used to investigate the effectiveness of prophylactic treatment with an HT2A receptor antagonist.

Publications

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