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Development of Revolutionizing Biomaterials Substituting Various Mammalian Organs by Means of Sintered Bioceramics

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Abstract

Development of biomaterials substituting various mammalian organs can be carried out by means of experimental evolutionary studies using collagen -hydroxyapatite composite, derived from adult cattle.

The evolution of the tissue-immune system can be studies by compound-ceramics of collagen-hydroxyapatite composite. Collagen-hydroxyapatite composite was sintered by high-pressure technique using collagen extracted from cattle skin, which had antigenicity [1,2]. Artificial bone marrow chambers were fabricated with the sintered collagen-hydroxyapatite composite. Experimental evolutionary studies using mammals (dogs) and chondrichthyes (sharks) were carried out implanting the chambers into their muscles [3,4]. The result showed that around the collagen composed chambers implanted into dorsal muscle of dogs, marked cell differentiation as well as dedifferentiation with atypia could be observed, which resembled a part the digestive tract of intestine histologically. Around the chambers implanted into dorsal muscle of sharks hemopoietic nests could be observed, which were quite similar to those induced by the chambers of conventionally sintered hydroxyapatite. Hemopoiesis and osteoid formation 4 months after surgery were observed around the collagen-apatite chamber implanted in the shark muscle as well as in upper site of vertebral cartilage of the spinal cord. No bone marrow in the cartilaginous tissue in upper site of the spinal cord is evident in control sharks. Xenotransplantation of skin, i.e., skin grafts between sharks of different kinds of species, as well as between sharks and xenopus (amphibian), sharks and mammals (rat) are carried out. All of them are successful and chimera placoids between them are developed. After that, the author successfully carried out xenotransplantation of various organs of chondrichthyes into those of dogs [5-7].

Introduction

The bone is definitive substance of the vertebrates. Therefore, using synthesized artificial osseous biomaterials trilateral riddles of the vertebrates, i.e., the evolutionary system, immune system, and development of bone marrow hemopoiesis can be read. Self and not-self immunology is in vogue in these days. However, this concept is defined only in tissue immunity. Present research aims to prove the development of tissue immunity via genetic expression by the gravity during

terrestrialization. In ontogeny, embryo has no tissue immunity, which is called immuno-tolerance. During research on phylogeny concerning bone marrow hemopoiesis the authors disclose that the function of human leukocyte antigen (HLA) is induced through the second evolution of the vertebrates, i.e., in terrestrialization conjugated with emergence of bone marrow hemopoiesis. The authors propose hypothesis in development of tissue immunity by increased gravity of 1G during landing or delivery from 1/6G in sea water or in amniotic fluid through phylogeny as well as ontogeny, to which organisms correspond by increasing blood pressure.

Materials and Methods

(1) Hydroxyapatite(HA) was sintered with collagen by high pressure gas technique at 40℃ with water. Artificial bone marrow chambers made of collagen-HA composite made of high-pressure sintering were fabricated by National Institute for Research in Inorganic Materials; collagen with antigenicity was extracted from cattle skin [1, 2].

(2) These chambers were implanted into mammals (dogs) as well as chondrichthyes (sharks). These were recovered 3 months postoperatively to make specimens. They were observed and these histopathological findings were compared.

(3) The following xenotransplantations between archetype and higher vertebrates are carried out.

A-Shark cartilage and muscle transplantation to two adult dogs (beagles).

B-Intestines of sharks to these of two adult dogs (shepherds).

C-Corneas of sharks to these of dogs

D-5 cases of a part of brains of sharks to these of rats

E-5 cases of a part of spine of cyclostomata to a part of rat femur nerves

Results

Collagen-hydroxyapatite composite was sintered by high-pressure low temperature technique using collagen extracted from cattle skin, which had antigenicity. Artificial bone marrow chambers were fabricated with the sintered collagen-hydroxyapatite composite. Experimental evolutionary studies using mammals (dogs) and chondrichthyes (sharks) were carried out implanting the chambers into their muscles. The artificial bone marrow chambers were implanted in dogs as well as in sharks of dorsal muscle.

The result showed that around the collagen composed chambers implanted into dorsal muscle of dogs, marked tissue differentiation with atypical cells could be observed, which resembled epithelium of digestive tract of the intestine histologically. Around the chambers implanted into dorsal muscle of sharks hemopoietic nests could be observed, which were quite similar to those induced by the chambers of conventionally sintered hydroxyapatite. From the experiments the authors disclosed chondrichthyes have no HLA (human leukocyte antigen) even though they have MHC (major histocompatibility complex). Therefore archetype vertebrates are in immuno-tolerance just like embryo of higher animals. To verify immuno-tolerance of chondrichthyes xenotransplantation of skin (skin graft) of sharks into mammals (rat) are carried out. After that, the author carried out xenotransplantation of corneas and brains of chondrichthyes into those of dogs as well as rats. All xenotransplantation between corneas (Figs 1-5) of sharks and those of dogs as well as xenotransplantation between a part of brains and those of rats (Fig 6) are successfully carried out. Neither rejection nor infection occurred. Histopathological findings show successful xenotransplantation of the intestine between dogs and sharks.

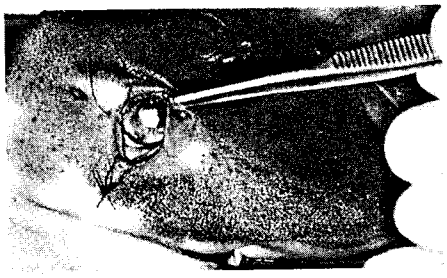

Fig. 1 Shark eye is being extirpated.

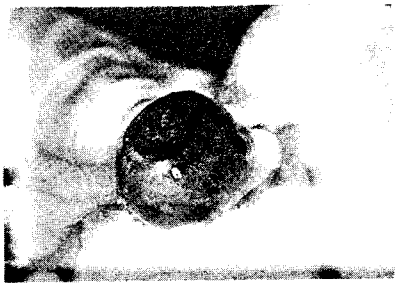

Fig. 2 Extirpated shark eye.

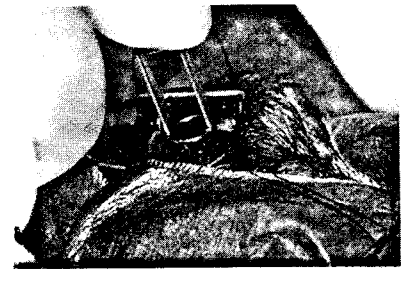

Fig. 3 Cornea of dog is being extirpated by trephine.

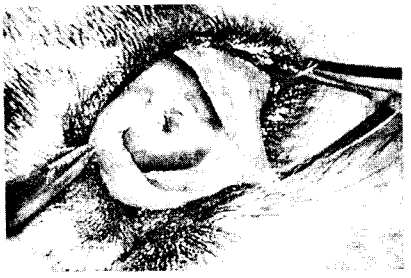

Fig. 4 Transplanted shark cones into dog eye, 2 weeks postop.

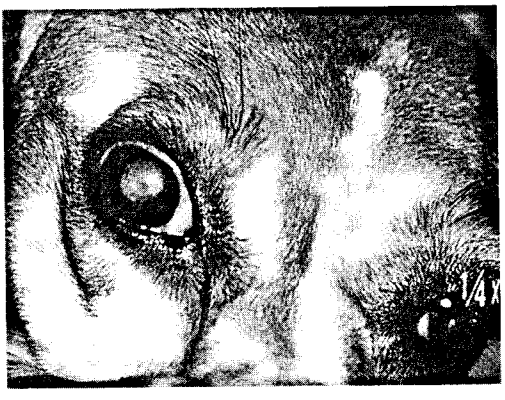

Fig. 5 Transplanted cornea, 3 months postop

Fig. 6 Successful xenotransplantation of shark brain into that of rat, 6 months postop.

Discussion and Conclusion

Haeckel proposed in his biogenetic law that ontogeny recapitulates phylogeny. Mammalians embryo has no tissue immunity, i.e., immuno-tolerance, even embryo has major histocompatibility complex (MHC). According to the biogenetic law archetype vertebrates chondrichthyes naturally has no tissue immunity. In sharks the major histocompatibility complex (MHC) of class I as well as class II are well known to exist. Therefore, in archetype vertebrates MHC is masked in genetic expression just as immuno-tolerance in embryos of higher animals.

As conclusion genetic expression of MHC is triggered by the gravity, which triggers the development of bone marrow hemopoiesis in phylogeny as well as in ontogeny. Without genetic expression of MHC xenotransplantation can be successfully carried out between the archetype vertebrates and mammals.

Therefore MHC exists not to distinguish self or not-self in organism but to function for cellular level digestion. From these experiments revolutionizing new biomaterials substituting allograft of various organs are developed for mammals.

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