

## Studies on Development of Biocompatible Biomaterials by Means of Experimental Evolutionary Studies

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Artificial bone marrow chambers made of collagen (with antigenicity)-HAP composite were developed and implanted into mammals as well as chondrichthyes. After that authors discover that archetype vertebrates chondrichthyes are in immuno-tolerance. Therefore, xenotransplantation between sharks and mammals can be done. Various organs and tissues of chondrichthyes are successfully transplanted into mammals. From these experiments new biomaterials are developed substituting organs or tissues.

**KEYWORDS:** Experimental Evolutionary study, Xenotransplantation, Immuno-tolerance, Biomaterials

### INTRODUCTION

It is known that primitive vertebrate chondrichthyes possess genomes of major histocompatibility antigen complex (MHC), however the authors have discovered that they have no tissue immunity. This means that they are in immuno-tolerance just as embryo of higher animals such as reptile, aves, and mammals. The author has successfully carried out skin grafts between different kinds of sharks, from *Heterodontus japonicus* (dog-shark) to *Triakis scyllia* (dochi shark). Skin grafts can also be carried out successfully from cyclostomata (hagfish) to rats, and the corneas of sharks can be successfully transplanted to the eyes of dogs. In addition, the intestine of sharks can be successfully transplanted to that of dogs. From these successful xenotransplantation, the major function of MHC (HLA) is found to be the cytological digestion system mainly functioning for tissue remodeling in the organism's own cells of organs, and partly to digest parasites and transplanted imported tissue.

### MATERIALS AND METHODS

- (1) Artificial bone marrow chambers of collagen-HAP composite made of high-pressure sintering were fabricated by National Institute for Research in Inorganic Materials; collagen with antigenicity was extracted from cattle skin <sup>1)</sup>.
- (2) These chambers were implanted into mammals (dogs) as well as chondrichthyes (sharks). These were recovered 3 months postoperatively to make specimens for histopathological observation.
- (3) The following xenotransplantation between archetype and higher vertebrates are carried out.

A- Shark cartilage and muscle transplantation to two dogs.

B- Intestine of sharks to that of two dogs.

C- Cornea of sharks to that of dog.

### RESULTS

The collagen-hydroxyapatite (artificial cartilage) artificial bone marrow chambers were implanted in shark muscle (Fig. 1). Hemopoiesis and osteoid formation 4 months after surgery were observed around the hydroxyapatite implanted in the shark muscle as well as in vertebral cartilage. On the contrary, in dog muscles around the artificial cartilage implanted marked tissue differentiation that resembled digestive tract formation could be observed <sup>2)</sup>. From these results the authors found sharks were in immuno tolerance. All xenotransplantation between organs of sharks and those of dogs are successfully carried out. Neither rejection nor infection was occurred. Histopathological findings show successful xenotransplantation between dogs and sharks of the intestine.

### DISCUSSION

From experiments of successful inducement of hemopoiesis with ossification of cartilage by collagen-HAP composite (artificial cartilage) implanted into dorsal muscle of sharks, it is disclosed that archetype vertebrates of chondrichthyes, i.e., sharks have no tissue immunity against cattle collagen with antigenicity. It is known that sharks have MHC. Therefore sharks are in immuno-tolerance just like embryo of mammals. After terrestrialization of chondrichthyes not only hemopoietic nest immigration from the gut system to

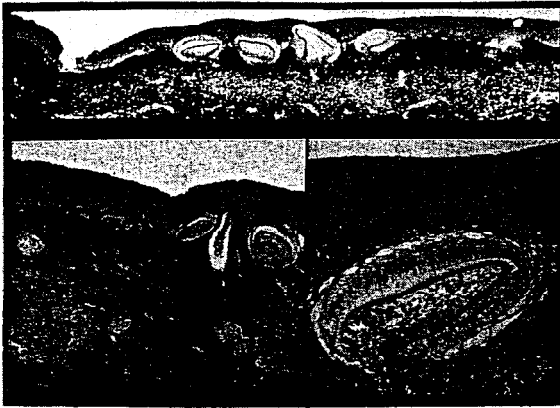


Fig. 1 Chimera placoids of shark and xenopus

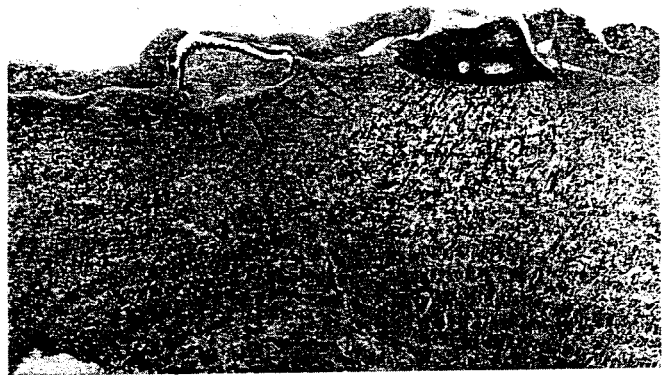


Fig. 4 Chimera placoids of shark and rat



Fig. 2 Shark placoids

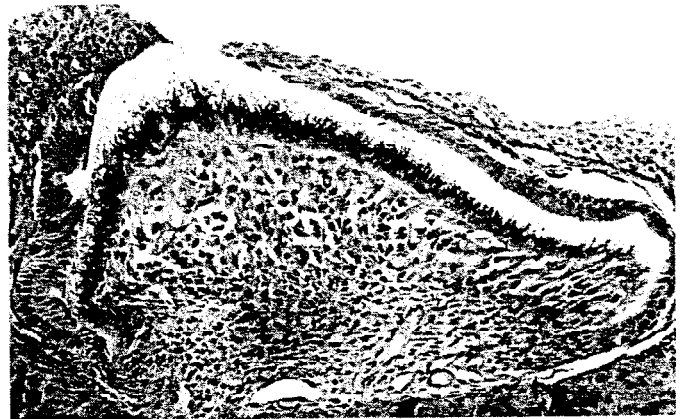


Fig. 5 Chimera placoids of shark and rat



Fig. 3 Chimera placoids of shark and rat

bone marrow occurred but tissue immunity by MHC was generated through reactions of sharks against increased gravity. To verify immune-tolerance of sharks xenotransplantation of xenopus as well as rat skin to that of sharks are carried out for preliminary experiment. Successful skin graft with chimera placoids formation between heterodontus and rat are fulfilled (Figs 2-5). After that xenotransplantation of shark cornea, muscle and intestine to those of dogs are successfully performed.

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