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4. Development of Hybrid-type Artificial Immune Organ by Means of Experimental Evolutionary Research Method Using Bioceramics

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Experimental evolutionary studies, applying biomechanical stimuli to biomaterials of sintered hydroxyapatite chambers in animal muscles, has been proposed by author by means of trilateral research method integrating morphology, physiology-biochemistry, and molecular genetics from the standpoint of biomechanics since 1995. Hybrid type artificial immune organ inducing hemopoietic bone marrow tissue could be successfully developed not only in mammals but in chondrichthyes (sharks), which are relicts of archetype without bone marrow tissue in internal skeletons. With these new method, *in vivo* culture of autogenous liver in hydroxyapatite chamber connected with femoral artery could also be successfully carried out in dogs.

The use and disuse theory of Lamarck has been revived due to molecular genetics recently. Alberch mentioned that the recapitulation theory (Haeckel) could be explained by heterochrony of gene expression. The use and disuse theory can also be explained by heterochrony, because all functions of muscle cells and osteocytes are controlled through gene expression of mesenchymal and neural cells, which are triggered by physicochemical stimuli (biomechanics in broad sense) effecting topical cells of the organisms. Therefore, evolutionary change of morphology in vertebrates can be understood caused by biomechanics as Lamarck mentioned from view point of trilateral research. For this reason, we can induce in heterospecies and heterotopically evolutionary changes at cellular level in mesenchyma through biomechanics. We refer to this new research method as experimental evolutionary study.

The Definitive substance of vertebrates is the hydroxyapatite-collagen complex skeletons, i.e., bone and tooth. The characteristic substance, which distinguishes lower vertebrates of chondrichthyes and cyclostomata from higher reptiles and mammals is the bone marrow cavity of inner skeletons with hemopoiesis. The characteristic organs, which distinguish mammals from other lower vertebrates, are highly evolved viscerocranium with gomphotic tooth and jawbones. In vertebrates, therefore, hydroxyapatite is an extraordinarily important substance with which, in combination with biomechanics, experimental evolutionary research method at cellular level can be developed. Through these new research methods new tissue engineering way has been developed as hybrid-type artificial immune organ and correlation between the system of immunity and metamorphosis (evolution) are investigated and a new concept of immunology as cytological digestion system and biomechanics-responding evolutionary theory are proposed.