Establishment of a new strategy for the treatment of functional restoration in skeletal muscle injury by tissue engineering using osteopontinederived SVVYGLR peptide

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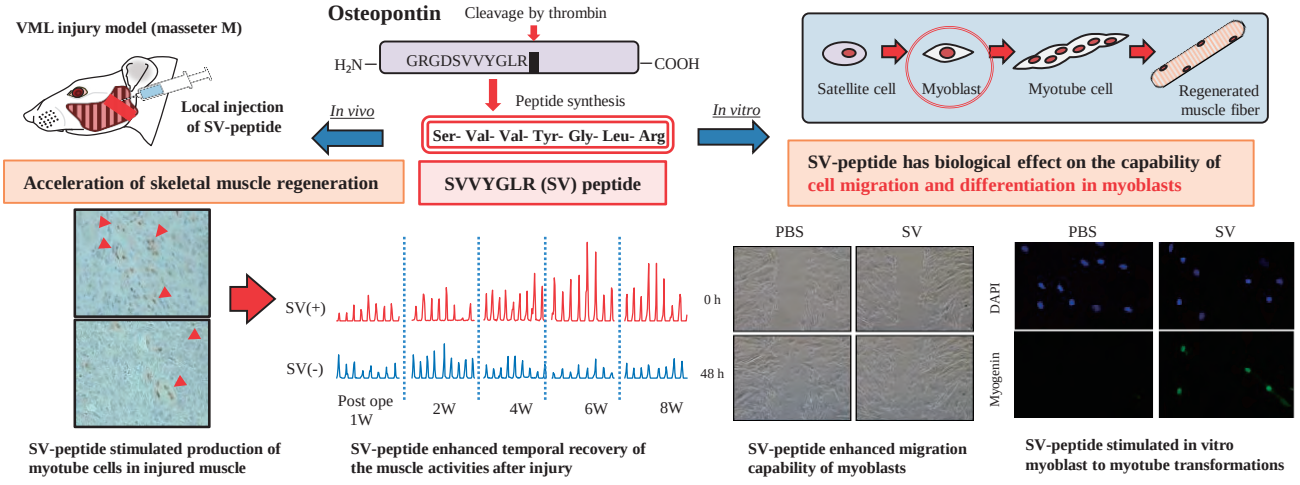
Project Outline

Skeletal muscle dysfunction with serious damages caused by injury or surgery, and congenital diseases with deformed or poorly developed muscular tissue such as cleft palate, conventional treatments including plastic surgery occasionally fail to obtain an adequate functional recovery. SVVYGLR (SV), 7-amino-acid sequence derived from osteopontin (SV peptide) has previously demonstrated strong angiogenic activity, enhancement of the synthesis of collagen type III in myocardial fibrosis and capability for improvement of cardiac function through the differentiation of fibroblasts to myofibroblasts. This peptide was also revealed to be easily degraded by peptidase and show less adverse effects, indicating high biocompatibility. Like myocardium, skeletal muscle is striated, but it is voluntary, composed of multi-nucleated muscle fibers regenerated by tissue-specific muscle stem cells called satellite cells which proliferate and differentiate to form mature myoblasts.

Given the potent role of SV peptide on the repair of injured skeletal muscles like myocardium, it might also contribute to functional restoration after the injury. Our preliminary study using rat volumetric muscle loss (VML) injury model in masseter muscles demonstrated that local injection of SV peptide immediately after the injury increased EMG activities recorded from injured muscles and suppressed fibrosis by the generation of scar tissues compared with injection of PBS or inactive form of SV. In addition, cultured human skeletal muscle precursor cells containing SV-peptide promoted the migration and differentiation of myoblasts.

Development roadmap

	2025	2026	2027	2028	2029	2030
GMP peptide synthesis	Estimation of efficacy Safety evaluation and pharmacokinetics Manufacturing process, quality control					
Non-clinical	Basic research (biological and physiological) Animal testing ADME discovery screening research (pharmacodynamics, pharmacokinetics, toxicity test)					
Phase I			Preparation of protocol, clinical study			
Phase II						
Phase III						
NDA						
Approval						



SV-peptide stimulated production of myotube cells in injured muscle

SV-peptide enhanced temporal recovery of the muscle activities after injury

SV-peptide enhanced migration capability of myoblasts

SV-peptide stimulated in vitro myoblast to myotube transformations

Target diseases in this project: Skeletal muscle injuries with irreversible motor dysfunction in oral and maxillofacial surgery, trauma, and congenital abnormalities including orofacial clefts such as cleft lip and palate. Title of the Invention: Restorative materials for skeletal muscle injury, Patent No. JP 6912117, US 11,077,167 B2 2017-229688. Aim of this project is to identify and develop a new novel peptide therapeutics with small molecule suited for functional regeneration in skeletal muscle injuries.