



## Learning from Bacteria to turn their Wisdom into Therapeutics

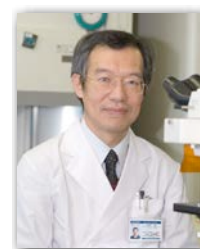


Fig. 1a

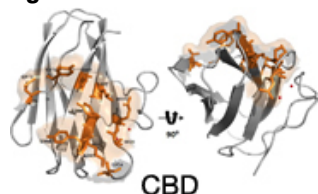
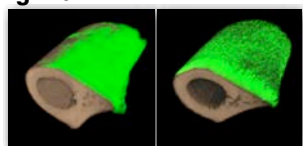


Fig. 1b



DBM+PBS DBM+GF-CBD

Fig. 2

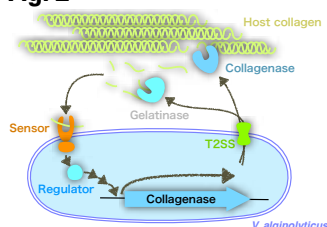
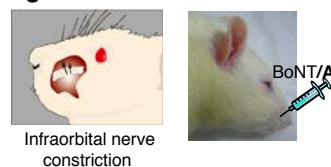


Fig. 3



Infraorbital nerve  
constriction



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### Research Interests:

#### 1. Histotoxic Clostridia

Collagens are the major protein constituents of the extracellular matrix. Histotoxic clostridia secrete collagenases that cause extensive tissue destruction in myonecrosis. The C-terminal collagen-binding domain (CBD) of collagenases is responsible for insoluble collagen fibril binding (Fig. 1a).

Although growth factors (GFs) are promising therapeutic agents, they have limited target specificity and short half-lives *in vivo*. To overcome these difficulties, we have produced fusion proteins consisting of GF moieties and CBD. The combination of GF-CBD with a collagen sheet or demineralized bone matrix induced periosteal bone formation at protein concentrations lower than those required for GF alone. We are pursuing preclinical studies to turn this idea into a reality in regenerative medicine (Fig. 1b).

(Collab. U. Arkansas, Kitasato U., Kagawa U., Waseda U., and Nippi)

#### 2. Vibrios

*Vibrio vulnificus* causes an infection commonly known as flesh-eating bacteria syndrome, and *V. alginolyticus* is a fish pathogen. Collagenase is one of the etiological agents produced by both pathogens to disrupt the host connective tissue. Production of collagenase in *V. alginolyticus* is inducible by its substrate collagen. This means that *V. alginolyticus* produces collagenase only when it infects the host, but not when it is present in the seawater. Using transposon random mutagenesis, a two-component regulatory system was identified to regulate the expression of collagenase (Fig. 2).

Our goal is to elucidate the whole mechanism of collagenase inducibility in *V. alginolyticus*. The medicine to inhibit the collagenase induction system could be a new anti-Vibrio infection agent. (Collab. U. Arkansas, and Waseda U.)

#### 3. Clostridium botulinum

*C. botulinum* strains produce immunologically distinguishable neurotoxins (types A-G) that cause a serious flaccid paralytic illness in humans and animals.

We are currently promoting the following researches:

- 1) Development of simple, sensitive and specific assay systems for botulinum toxin detection to replace the mouse bioassay (Collab. Waseda U., and Kanto Chemical Co., Inc.)
- 2) Clinical application of botulinum toxin type A in the treatment of trigeminal neuralgia (Fig. 3) (Collab. Tokushima U., and Dental Sch., Okayama U.)
- 3) Structure-function relationship of botulinum toxins.

### International Education Programs:

We have been accepting undergraduate/graduate students from University of Arkansas, U. S. A., and Udayana University, Indonesia into short programs with enthusiastic assistance of Udayana Faculties/Okayama Grad Students (Dr. N. N. Dwi Fatmawati and Dr. Agus E. Darwinata).

**Basic Research Bldg. 7th Floor. Turn 3 times Left. Our Door is always OPEN.**