

## UPDATE FROM THE CUTTING EDGE

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The abstracts of the recent research information appearing in Vol.8 No.1-3 of "AIST TODAY" are introduced here, classified by research area. For inquiry about the full article, please contact the author via e-mail.

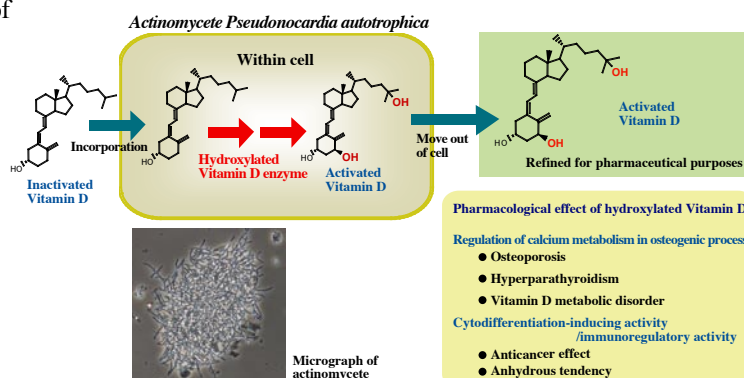
Life Science & Technology

### Isolation of enzyme involving in activation of vitamin D

#### High-efficient production of hydroxylated vitamin D used for pharmaceutical purposes

It has been known that vitamin D<sub>3</sub> (VD<sub>3</sub>) is hydroxylated in liver and kidney by cytochrome P450 monooxygenases (CYPs) in animals, resulting in the formation of 1 $\alpha$ , 25-dihydroxy VD<sub>3</sub> (calcitriol) which modulates calcium metabolism. Calcitriol and its derivatives are used as pharmaceuticals for rickets, osteoporosis and parathyroidosis. About 20 processes are, however, required in chemical synthesis of calcitriol and its yield is very low. Alternate production of calcitriol is carried out by the use of an actinomycete *Pseudonocardia autotrophica* as a converter; the cell efficiently converts VD<sub>3</sub> to calcitriol by endogenous CYP. We therefore isolated the CYP involved in the VD<sub>3</sub> hydroxylation (VDH) and subsequently cloned the corresponding gene from *P. autotrophica*. Conversion of VD<sub>3</sub> to calcitriol was observed using recombinant VDH and its redox partners in an *in vitro* reconstitution assay. We also confirmed that *Rhodococcus* cells expressing VDH and redox partner proteins were capable of the biotransformation of VD<sub>3</sub>. Mutational engineering of the *vdh* gene and genetic engineering of appropriate host cells will dramatically improve the productivity of hydroxylated VD<sub>3</sub>s in the near future.

\*This is the result of a joint research with Mercian Corp. (Iwata, Japan).



Activation of vitamin D by actinomycete and pharmacological effect of hydroxylated vitamin D

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