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EDITORIAL

First JA Medal goes to a paper on decalpenic acid

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The Editorial Board of *The Journal of Antibiotics* has awarded the inaugural *Journal of Antibiotics* Medal to the authors of the original article entitled 'Decalpenic acid, a novel small molecule from *Penicillium verruculosum* CR37010, induces early osteoblastic markers in pluripotent mesenchymal cells' (Shuichi Sakamoto, Fukiko Kojima, Masayuki Igarashi, Ryuichi Sawa, Maya Umekita, Yumiko Kubota, Koichi Nakae, Shoichi Yamaguchi, Hayamitsu Adachi, Yoshio Nishimura and Yuzuru Akamatsu) that appeared in the journal in 2010, volume 63, pages 703–708.[1] In this paper, the authors report the structure and biological function of decalpenic acid, a polyketide natural product with fascinating ability to induce differentiation of mesenchymal stem cells toward osteoblast lineage.

Osteoblasts are foundational cells essential for bone formation.[2] Among many tasks vital to bone metabolism, osteoblasts produce osteoid, a complex of proteins including Type 1 collagen that forms the primary organic elements of bone. Osteoblasts are also required for osteoid mineralization and overall strengthening of the bone material. The essential role of osteoblasts in bone physiology often makes them central players in bone disease, including osteoporosis and cancer.

The differentiation program that gives rise to osteoblasts from progenitor mesenchymal cells where the canonical Wnt signaling pathway has a major role. Several signaling factors and molecular markers map the differentiation of mesenchymal cells along the osteoblast lineage.[3] Small molecular probes of this pathway have great value in assisting in unraveling the molecular details of differentiation and also have potential as leads for drugs.

In their *Journal of Antibiotics* Medal paper, the winner's group have discovered a fungal metabolite, decapenic acid, that is an inducer of early-stage markers of osteoblast differentiation.[1] Using a screen of a mouse mesechymal cell line for the osteoblast marker alkaline phosphatase (ALP), the authors identified an extract from the fermentation broth of the fungus *P. verruculosum* CR37010 with the desired ALP induction phenotype. Activity guided purification from a 10 kg culture broth provided 8.4 mg of the active substance, a polyketide termed decalpenic acid. Decalpenic acid is composed of a central bicyclic ring decorated with a propyl group and a tetraenoic acid. Careful NOE experiments revealed the relative stereochemistry and demonstrated that the pending propyl and a tetraenoic acid groups were on the same face of the bicyclic ring.

The paper goes on to explore the biological activity of decalpenic acid. Using a series of molecular markers of mesenchymal differentiation, along with the control synthetic compound purmorphanine, which has been also shown to be an osteoblast and ALP inducer via the hedgehog pathway,[4] the winner's group show that decalpenic acid acts at the early stages of osteoblast formation providing a novel probe to explore bone physiology and a new chemical biology tool for the study of a vital cellular programs.

Gerard D Wright and Minoru Yoshida
Review Editors,
The Journal of Antibiotics

ABOUT THE WINNER

The First Author Dr Shuichi Sakamoto received his PhD degree from the Graduate University for Advanced Studies [SOKENDAI] in 2001 for his study of premature aging Werner syndrome under the supervision of Dr Yasuhiro Furuichi (AGENE Research Institute). He also worked with Dr Furuichi as a postdoctoral fellow from 2001 to 2002. He then moved to Kyoto University as an Assistant Professor to work with Professor Kenshi Komatsu in the field of radiation biology from 2002 to 2005. In 2005, he joined the Institute of Microbial Chemistry as a researcher and started working in the field of natural products and chemical biology. His current research interests include chemical biology of mesenchymal stem cell and cancer metastasis.

About JA Medal: This new award program was established in 2011 to acknowledge the articles of highest impact and recognition, selected from among all original articles published in the *Journal of Antibiotics*. The JA medal will honour the authors of such articles for their excellent research results that have contributed to the development of antibiotics studies and will hopefully encourage submission of quality original articles to the journal. All original articles published in JA are automatically nominated for the award. Next JA medal winner will be selected in 2013 from the articles published in 2010–2012.

1 Sakamoto, S. *et al.* Decalpenic acid, a novel small molecule from *Penicillium verruculosum* CR37010, induces early osteoblastic markers in pluripotent mesenchymal cells. *J Antibiot* **63,** 703–708 (2010).
2 Caetano-Lopes, J., Canhao, H. & Fonseca, J. E. Osteoblasts and bone formation. *Acta Reumatol Port* **32,** 103–110 (2007).
3 Marie, P. J. Signaling pathways affecting skeletal health. *Curr Osteoporos Rep* **10,** 190–198 (2012).
4 Wu, X., Walker, J., Zhang, J., Ding, S. & Schultz, P. G. Purmorphamine induces osteogenesis by activation of the hedgehog signaling pathway. *Chem Biol* **11,** 1229–1238 (2004).