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# **EIGHTH INTERNATIONAL SYMPOSIUM ON THE BIOLOGY OF VERTEBRATE SEX DETERMINATION**



**April 16-20, 2018 KONA, HAWAII**

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**16-20, APRIL 2018**

**King Kamehameha's Kona Beach Hotel**

**Kailua-Kona, Hawaii**

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**Cover:** Statue of Ardhanarishvara, the half-male, half-female form of Shiva, India 11<sup>th</sup> century A.D.

# SOX5 IS INVOLVED IN GERM CELL REGULATION AND SEX DETERMINATION IN MEDAKA FOLLOWING CO-OPTION OF NESTED TRANSPOSABLE ELEMENTS

Manfred Schartl<sup>1, 2, 3</sup>, Susanne Schories<sup>1</sup>, Yuko Wakamatsu<sup>1</sup>, Yusuke Nagao<sup>4</sup>, Hisashi Hashimoto<sup>4</sup>, Chloé Bertin<sup>7</sup>, Brigitte Mourot<sup>7</sup>, Cornelia Schmidt<sup>1</sup>, Dagmar Wilhelm<sup>5</sup>, Lazzaro Centanin<sup>6</sup>, Yann Guiguen<sup>7</sup> and Amaury Herpin<sup>1, 7</sup>

<sup>1</sup> University of Wuerzburg, Physiological Chemistry, Biocenter, 97074 Wuerzburg, Germany.

<sup>2</sup> Comprehensive Cancer Center Mainfranken, University Hospital, 97080 Wuerzburg, Germany.

<sup>3</sup> Texas Institute for Advanced Study and Department of Biology, Texas A&M University, College Station, Texas 77843, USA

<sup>4</sup> Bioscience and Biotechnology Center, Nagoya University, Furo-cho, Chikusa-ku, Nagoya, Aichi, Japan.

<sup>5</sup> University of Melbourne, Department of Anatomy & Neuroscience, Parkville, Victoria 3010, Australia.

<sup>6</sup> University of Heidelberg, Centre for Organismal Studies (COS), Heidelberg, Germany.

<sup>7</sup> INRA, UR1037 Fish Physiology and Genomics, F-35000 Rennes, France.

Sex determination relies on a hierarchically structured network of genes, and is one of the most plastic processes in evolution. The evolution of sex-determining genes within a network, by neo- or sub-functionalization, also requires the regulatory landscape to be rewired to accommodate these novel gene functions. We previously showed that in medaka fish, the regulatory landscape of the master male-determining gene *dmrt1bY* underwent a profound rearrangement, concomitantly with acquiring a dominant position within the sex-determining network. This rewiring was brought about by the exaptation of a transposable element (TE) called *Izanagi*, which is co-opted to act as a silencer to turn off the *dmrt1bY* gene after it performed its function in sex determination.

We now show that a second TE, *Rex1*, has been incorporated into *Izanagi*. The insertion of *Rex1* brought in a preformed regulatory element for the transcription factor *Sox5*, which here functions in establishing the temporal and cell-type-specific expression pattern of *dmrt1bY*. Mutant analysis demonstrates the importance of *Sox5* in the gonadal development of medaka, and possibly in mice, in a *dmrt1bY*-independent manner. Moreover, *Sox5* medaka mutants have complete female-to-male sex reversal. Our work reveals an unexpected complexity in TE-mediated transcriptional rewiring, with the exaptation of a second TE into a network already rewired by a TE. We also show a dual role for *Sox5* during sex determination: first, as an evolutionarily conserved regulator of germ-cell number in medaka, and second, by *de novo* regulation of *dmrt1* transcriptional activity during primary sex determination due to exaptation of the *Rex1* transposable element.