Some like it hot...some don't

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Video Abstract

Keywords: Science, Duke University Medical Center, Zhejiang Wanli University, STAT3, Kdm6b, calcium signaling, temperature-dependent sex determination, Trachemys scripta elegans, red-eared slider turtle, post-translational modification, phosphorylation, female-producing temperature, male-producing temperature, thermosensitivity, pSTAT3, gonads, transient receptor potential, TRP channel, environmental sensor, TRPV4

Posted Date: October 23rd, 2020

DOI: https://doi.org/10.21203/rs.3.rs-97524/v1

Abstract

A change in temperature can easily alter the course of our day. But for some reptiles and fish, it can set the course of their lives—deciding whether they emerge as male or female when they hatch. Basically, temperature affects whether the early gonad becomes a testis (making male hormones) or an ovary (making female hormones). It's called temperature-dependent sex determination, and it was first described in the late 1960s. But only now are researchers close to understanding how this phenomenon works on a molecular level. A new study reveals the genetic circuitry behind this type of sex determination in red-eared slider turtles. Researchers recently discovered the role played by an epigenetic regulator known as KDM6B, which can control whether a gene is turned on or off. KDM6B is required for the expression of the sex-determination gene Dmrt1, which leads to a male anatomy. When KDM6B is absent, as it tends to be at higher temperatures, male genes are not activated, and would-be testes transform into ovaries. Interestingly, expression of the Kdm6b gene is temperature-sensitive; the gene is only highly expressed at cool temperatures, which leads to the formation of males. So what controls Kdm6b expression? The research team zeroed in on the protein STAT3 . In other tissues, when decorated with a phosphoryl group, STAT3 — now pSTAT3 — can switch Kdm6b expression off. Could this be happening in the turtle gonad? The group showed that STAT3 is only phosphorylated at the high female-producing temperature. To test whether pSTAT3 represses Kdm6b, researchers blocked the protein in gonads from red-eared slider embryos incubating at male or female temperatures. This experiment had no effect on gene expression at the lower male temperature. But at the higher temperature, which normally activates pSTAT3 and sets the genetic gears in motion to produce females, levels of pSTAT3 dropped. And the expression of Kdm6b and the male-determining gene Dmrt1 increased. Those findings were replicated in living turtle embryos: of 23 eggs incubated at the higher, female producing temperature and treated with a pSTAT3 inhibitor, 16 showed an ovary-to-testis shift in sexual trajectory. So is pSTAT3 the ultimate lever when it comes to temperature-dependent sexual determination? Not quite. Further experiments highlighted the central role played by calcium channels. Using a calcium dye, the researchers visualized how much calcium was in turtle gonad cells at different temperatures. With increasing temperature, the cells became brighter, indicating an increase in calcium. But it isn't yet clear exactly which ion channels are in control, or whether calcium directly or indirectly promotes the activation of STAT3. Temperature-dependent sex determination is a fascinating example of how a varying environmental signal translates into a permanent change in gene activity and tissue identity. This isn't unique to turtles either. Lots of animals, including humans, experience changes in gene expression in response to stress and other life events. Reliance on temperature-dependent sex determination has grave implications for many species in this era of global warming. Scientists hope that a better understanding of this process may improve our ability to intervene and support species' adaptation and survival. This material is based upon work supported by the National Science Foundation under Grant Number 1854642. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the National Science Foundation.