## Milestones of the biomedical research with Clawed Frogs

For nearly one hundred years, the clawed frogs have provided answers to essential biological processes. In the timeline you can find the most important groundbreaking developments and successes that have shaped biomedical research.

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The studies on frog embryos carried out in the 1920s by Hans Spemann and Hilde Mangold show that certain cell groups (organizer cells, Spemann-Mangold organizer) can influence the development of the surrounding cells into different body parts. This study is fundamental for the understanding of cell differentiation in the field of development. Hans Spemann received the Nobel Prize in 1935 for Physiology or Medicine for this discovery.

First pregnancy test (pharmacist's frog) In his work from 1962, John B. Gurdon studied embryonic development by implanting the differentiated intestinal epithelial cells of tadpoles into frog eggs after removing the egg nuclei. This study is fundamental to understanding that nuclei of fully developed cells can be reprogrammed to give rise to other fully developed cell types. In 2012, together with Shinya Yamanaka, he was honored with the Nobel Prize for Physiology or Medicine, which led to advancements in stem cell research.

Discovery of factors that regulate the cell cycle

In order to demonstrate their function as water channels, in 1992 Peter Agre studied aquaporins on frog eggs, which are normally impermeable to water. This study is of fundamental importance in terms of understanding how the kidneys regulate their water balance. He was awarded the Nobel Prize in Chemistry in 2003, which led to advances in research of kidney diseases.

Long-term limb regeneration in adult frogs

1920s

1962

1992

1930s - 1960s

Discovery of the organizer effect in embryonic development

Lancelot Hogben (1930) and Hillel Abbe Shapiro & Harry Zwarenstein (1933) independently reported that adult female frogs can be used to determine pregnancy in humans. For this purpose, the urine of potentially pregnant women were injected into the frogs - if the frogs spawned within 16 - 18 hours, a pregnancy was indicated. This method was used until the development of immunochemical tests in the 1960s.

Discovery of the cell nucleus reprogramming in fully developed cells

1971 - 1990s

The first discovery of mitosis promoting factor (MPF) which initiates the cell cycle, was made in 1971 by Yosio Masui and Clement Markert. Tim Hunt later investigated further factors such as cyclins, in the 1980s and 1990s in many model organisms, including frog eggs, and discovered that cyclins are indeed part of the MPF complex. He was awarded the Nobel Prize in Physiology or Medicine in 2001 for his contributions in this field, and it is now known that these factors also play a role in cancer cells.

Discovery of the water channels function in cell membranes

2022

The scientists at Tufts University in the USA have shown that they can restore the form and function of a hind limb of adult clawed frogs using a portable system for administering multiple drugs. This is an important step in biomedicine, as adult clawed frogs, like humans, have limited regenerative abilities. This approach led to the growth of complex tissue consisting of skin, bones, muscles and nerves. This study is important as it could help millions of patients who, for instance, have lost limbs due to diabetes.

