Stem cell-based therapy for corals

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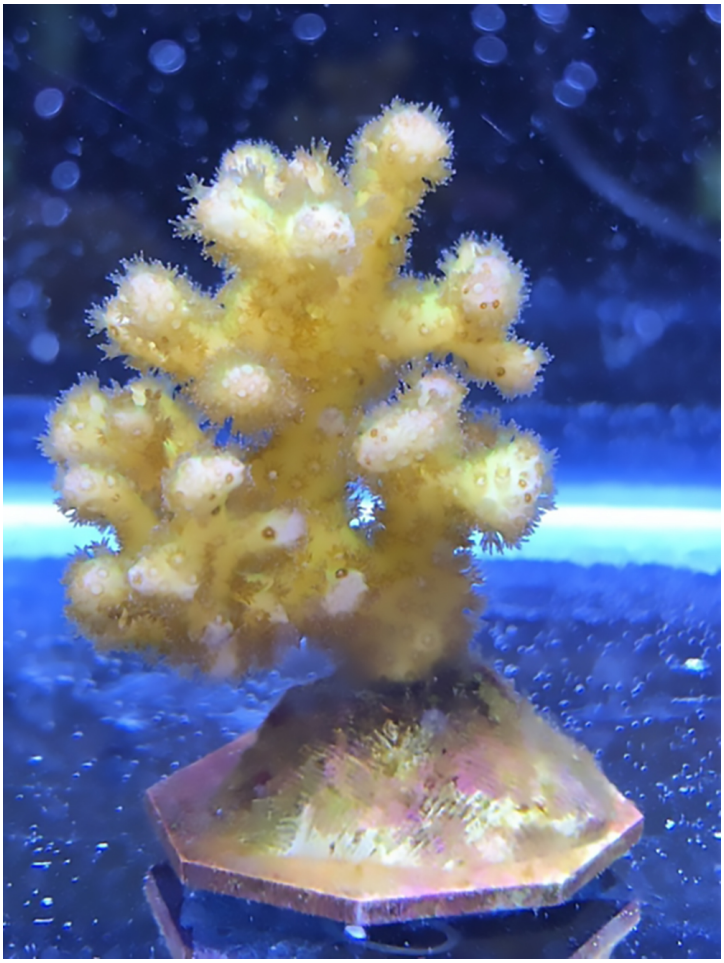
Could medical approaches of stem cell-based therapy, be a tool for corals' resilience to heat stress? Benyamin Rosental, Principal Investigator, Assistant Professor at Ben Gurion University of the Negev in Israel answers the compelling question here

Our laboratory at Ben Gurion University of the Negev in Israel is concerned with immunology and focuses on transplantation immunology, mainly at the immune cell level. We focus on stem cell transplantation, specifically on the blood-forming stem cells, termed "bone marrow transplantation".

Cellular immunology laboratory for corals

The uniqueness of our laboratory at Ben Gurion University of the Negev is that we use comparative/evolutionary approaches to understand the basic conserved mechanisms in transplantation immunology. Our undoubted expertise in the field provides us with the tools to isolate stem cells and immune cells in organisms, something that wasn't previously possible to do. Through our collaborative work, we have established two significant projects to help us understand cellular immunology and use stem cell therapies for corals. Our first project concerns testing the hypothesis that the coral immune system is under heat stress, which is part of the "coral bleaching" phenomenon.

Our second project concerns developing stem cell transplantation for corals as a potential tool for cell therapy. This is comparable to bone marrow transplantation in humans, when we take healthy blood-forming stem cells from a donor and transplant them to an individual with immune white blood cells deficiency so they can develop a healthy immune system. In corals, we would do that from a heat stress resilient individual coral to a sensitive one. In this profile, we will explain how these two projects came about in an immunology laboratory in Israel, as well as the logic behind our research ideas.



The coral Pocillopora damicornis. By Mike Connelly.

Coral reefs under threat

Coral reefs are basic ecosystems, important for marine life as well as human local communities. Unfortunately, during recent decades, the coral reefs are in steady decline due to human-associated stress, mainly heat stress conditions. Coral reefs are based on stony corals, which are colonial animals that create a calcium-based skeleton which is the base of the coral reefs, physically and ecologically.

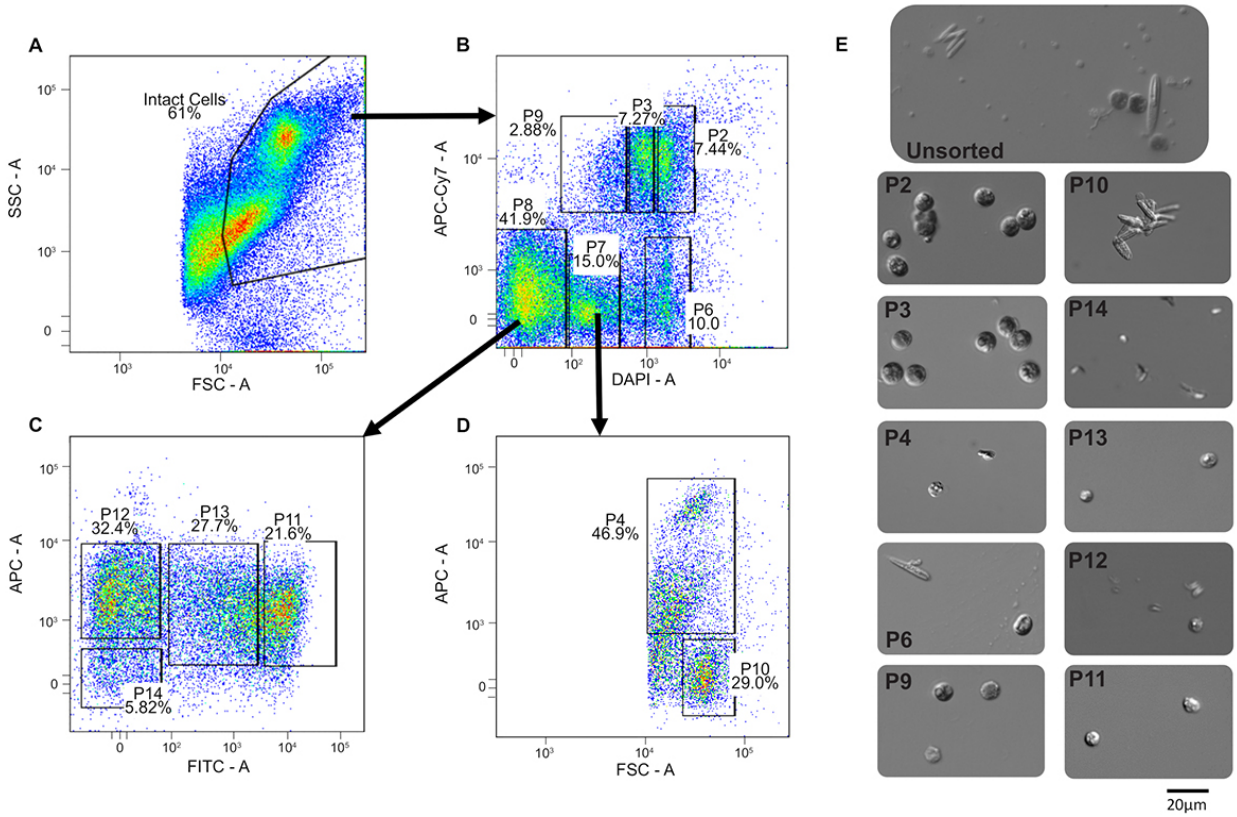
Some of those animal colonies live for tens and even hundreds of years and can reach diameters of several metres. A coral reef is built on many of those animals. Corals also contain symbiotic algae, which provide them with nutrients. In severe and prolonged heat stress, the symbiosis is broken and the algae leave the coral tissues, which leads to coral bleaching and eventually the death of the coral.

Optional tools for coral conservation

There is a big effort taking place in the scientific community and conservation groups to seek solutions for declining coral reefs globally. The basic tools to reduce stress on corals are reducing pollution, global warming, and the stress from fisheries and physical disturbance. But those approaches are not enough, because due to global warming, even remote reefs are under threat and have had severe bleaching effects during recent years.

Interestingly, there are individuals of the same species that are more tolerant to die-offs due to heat stress. About 10% of corals do survive in such conditions, which means they have resilience genes that make them more durable to those stressors. Many of the ideas are based on the use of those individuals to renew the coral reefs. The basic one is to make breeding using those resilient corals, in the same way as plant breeding for agriculture.

Additionally, since corals are colonial animals, a fraction of the coral can also grow a new one. The main problem with it is the time taken for corals to grow, depending on the species, but a few centimetres a year is the maximum. This means that to renew a reef will take many decades, but this is still a start. And the big question remaining is how can we help an existing coral which could be a hundred years old and the size of a small car to stand against a future heatwave?



Isolation and sorting of cell populations from the coral Pocillopora damicornis (Snyder et al., 2020).

Stem cell-based therapy

The approach of trying to transfer the characteristic of the resilient individual corals is at the heart of our research. This can go in two directions; one is directly transferring stem cells with the resilience genotypes and their genes which enable resilience, as done in humans with bone marrow transplantation for more than 45 years now. The second direction concerns understanding which genes are enabling resilience to some individuals, this we believe is the key.

Several laboratories are working on understanding the genes which are enabling heat resilience. When this is solved, we will need a tool for transferring those genes to existing corals: this is called gene therapy and today, it is achieved by isolating stem cells from an

individual, changing the target genes and transplanting them back. Both of those directions are based on the ability of isolation and transplantation of stem cells from and to adult coral animals. Certainly, those are the tools we are developing in our laboratory.

Stem cells are self-renewing cells that live throughout the entire life of an organism and are capable of renewing tissues and different cells of the body. They will carry their original genes for life and create cells and tissues with the same characteristics, including, in this case, heat resilience.

How the project came about

During my postdoctoral research at Stanford University in the U.S., I was stationed between the Medical School and the Hopkins Marine Station and carried out comparative transplantation immunology on the marine model organism. At that point, Dr Traylor-Knowles was a Postdoctoral Researcher working on the genetic response of corals to heat stress and bleaching. She discovered that immune genes were upregulated in response to heat stress. Dr Traylor-Knowles and I then started working together on developing the tools for isolating coral cells and characterising their immune system.

This research work continues with close collaboration, where we test the corals' immune responses in heat stress. This project is supported by the NSF-BSF Integrative and Organismal Systems (IOS) grant. Interestingly, during this research work, we have isolated candidate coral stem cells, and that intrigued the Revive & Restore conservation organisation, which made us a part of the Advanced Coral Toolkit program. Revive & Restore is the leading non-profit conservation organisation promoting the incorporation of biotechnologies into standard conservation practices and they are based in Sausalito, California, in the U.S. https://reviverestore.org/corals.

The project we started in 2021 in our laboratory came about from the research ideas of cellular immune and stem cell work in corals. In this Research Program, we develop tools for the isolation, characterisation and transplantation of coral stem cells. We are developing the tools for stem cell transplantation in anemone models (species related to corals), and the next steps will concern different stony corals.

Please Note: This is a Commercial Profile

Stem cell isolation and transplantation in Hexacorallia: Toward cell-therapy for corals. ERC-2020 Starting grant, #948476 CoralStem.