

A new beat in heart research

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Sudden Cardiac Arrest syndrome (SCA) is poorly understood, but it's a real danger for the otherwise young and healthy. For no apparent reason, the heart suddenly stops beating, and without treatment death may follow within minutes. It's why some athletes drop dead on the track and why a young man, without any warning, suddenly dies while sitting at his desk. SCA accounts for approximately 300,000 deaths per year in the U.S.

Dr. Joel Hirsch of Tel Aviv University's Department of Biochemistry has teamed up with Prof. Bernard Attali of TAU's Sackler Faculty of Medicine Department of Physiology and Pharmacology to investigate the cause and effects of the fatal syndrome. Not the same as a heart attack — in which heart muscles continue to pump, however erratically — SCA normally occurs with no warning.

This team is hot on the trail of understanding how a multi-gene syndrome, one of the causes for SCA, operates inside the body. Once they figure out how the disorder operates and describe its molecular system in detail, they hope to develop a drug or therapy to stop this condition before it strikes.

Solving the mystery of sudden death

"SCA is not as uncommon as most people think," Dr. Hirsch says. "It may explain a lot of mysterious occurrences in which people, even very young people, drop dead for no apparent reason. Doctors have started screening athletes for this condition, which can be exaggerated under physical exertion. Our research into the biological mechanisms of SCA



can add to the toolbox of diagnostic possibilities — and we hope that it will help science find a new drug to treat it.

"We are looking specifically at channels that allow certain electrical ions to pass through membranes, and the mutated ones that do not. If we can understand the molecular signalling required to keeping the heart pumping regularly, we might be able to design a drug to help cure the disease before it strikes," says Dr. Hirsch.

The answer lies in the molecular machinery of the cell, Dr. Hirsch explains. "There are mutations that can be found when doctors do genetic screening called Long QT syndrome. We are trying to figure out what has gone awry in the signaling systems in people with these mutations, starting with how the natural nanomachines work," he explains.

How cell membranes communicate

So far, Dr. Hirsch's team has mapped the molecular structure of some modules of the important communicators in cell membranes, and they are now investigating how signals can be blocked or turned on to prevent SCA. Currently the only treatment for SCA is to use the defibrillators found in public places, such as airports, which must be used within minutes.

"Our goal is to get to the part of the protein channel which is easily 'druggable' — that is an effective target for drugs. So far, we've been able to show how this communication channel assembles, and we are extending our focus to see how the molecular structure looks, explaining in atomic detail how mutations cause the disorder."

The same and similar mutations, he says, can also lead to deafness and epilepsy, suggesting that his research is applicable to a number of



significant and currently incurable conditions.

Provided by Tel Aviv University

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