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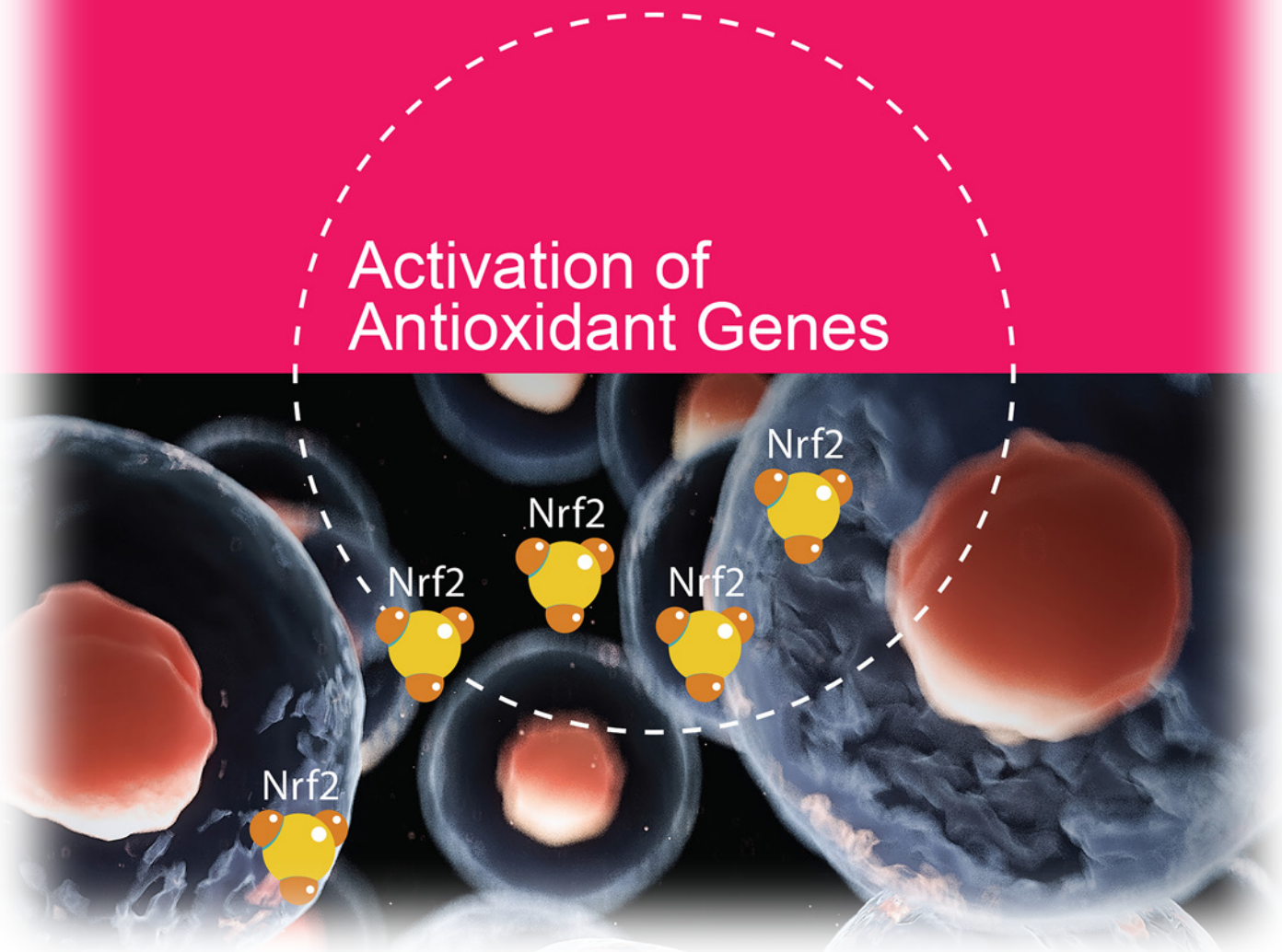
Towards Treating OXIDATIVE STRESS



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Front Cover:

Arie Gruzman and co-workers

Computer-Aided Design and Synthesis of 1-{4-[(3,4-Dihydroxy-benzylidene)amino]phenyl}-5-oxopyrrolidine-3-carboxylic Acid as an Nrf2 Enhancer

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CHEMPLUSCHEM Cover Profile

Computer-Aided Design and Synthesis of 1-{4-[(3,4-Dihydroxybenzylidene)amino]phenyl}-5-oxopyrrolidine-3-carboxylic Acid as an Nrf2 Enhancer


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Invited for this month's cover is Prof. Arie Gruzman (Bar-Ilan University) and collaborators who have developed an Nrf2 enhancer. This compound activated the Nrf2 transduction pathway and because of this the translation of dozens of antioxidant cytoprotective proteins in a dose- and time-dependent manner and protected PC-12 cells against oxidative stress. Considering the imbalance between production and elimination of oxidative species involved in the pathophysiology of many human diseases, this compound is a promising starting point for the development of novel therapeutics for the treatment of oxidative-stress-related diseases. Read the full text of the article at 10.1002/cplu.201700539.

What prompted you to investigate this topic?

We were amazed by our preliminary results that led us to use constant activation of Nrf2 as a general inducer of the entire cellular antioxidant system. This single protein can induce the transcription of dozens of antioxidant genes. Under physiological conditions, this transcription event happens only if cells need protection against oxidative stress. The main aim of the project was to design a compound that would "turn on" this system even when the level of oxidative species was not so high. Such a compound could protect human cells in a situation where the Nrf2 system is not activated enough. Moreover, the compound might be used as a potential antiaging agent. It is no secret that the progress of human life can be described as the slow oxidation of our cells, thus a decrease in the level of free radicals, even in physiological conditions, would go a long way to prolonging the human life span.

How cooperation of three research group from same department at Bar-Ilan University contributes to successful multidisciplinary research?

Chemistry is such a diverse science that in the same chemistry department people work in totally different fields of this discipline. In our case, Prof. Shai Rahimipour was the expert in biochemistry, Prof. Hanoch Senderowitz was responsible for the in silico part of the research, and Prof. Gruzman specialized in organic synthesis. There is no doubt that our daily interactions to exchange ideas and discuss results promoted better scientific outcomes for this project. With the help of other collaborators from Israel (Dr. Guy Cohen and Prof. Daniel Offen), the USA (Prof. Ben Major), and P. R. China (Dr. Zhengyu Jiang) this project, which required diverse expertise and a multidisciplinary approach, led to the successful development of a novel antioxidant molecule.

What do you consider exciting developments in the field?

Recent developments in the field of antioxidative stress therapy and antiaging agents are indeed very impressive. Among them, specifically navigated to mitochondria antioxidant molecules and the discovery critical for the antioxidant and antiaging response proteins such as SIRT6. In addition, a new opportunity for the possible pharmacological intervention into epigenome for decreasing of the oxidative stress, which lead to prolonging the lifetime of the entire organism, is very exciting.