

Can several Nobel Prizes be wrong?

New insights into Heterotrimeric G proteins signaling

Jimmy Botella, University of Queensland, Australia

Heterotrimeric G proteins (G-proteins), composed of α , β and γ subunits, are essential signaling molecules in most living organism. In humans, G-proteins control vision, smell, taste, and dysfunctions on their signaling cause diseases such as cholera and cancer. In animals and fungi, G-protein-coupled receptors activate signaling by binding GTP to the $G\alpha$ subunit and signaling stops when the GTPase activity in $G\alpha$ hydrolyzes GTP to GDP. This mode of action has been universally accepted since Alfred Gilman and Martin Rodbell were awarded the Nobel Prize in 1994. Our work on plant G-proteins has produced numerous surprises and proven that plant G-proteins evolved much faster than their animal counterparts [1], developing new and atypical subunits [2, 3], and adopting novel functions controlling important agricultural traits [4]. Our new results have added the greatest surprise so far: Plant G-proteins do not necessarily use GTP (or any other nucleotide) to exert their functions in plants [5]. We will present evidence showing the plant G-proteins can mediate signaling in a nucleotide independent manner. Point mutations in the *Arabidopsis thaliana* $G\alpha$ subunit were produced in order to abolish nucleotide binding without affecting their 3D structure. These mutations were used to complement $G\alpha$ -deficient mutants with full restoration of many, but not all, mutant phenotypes. In addition, our CRISPR generated G-protein mutations in tomato have shown that G-proteins have a much important role in plant defense than previously thought.

[1] Urano, D., Maruta, N., Trusov, Y., Stoian, R., Wu, Q.Y., Liang, Y., et al. Saltational evolution of the heterotrimeric G protein signaling mechanisms in the plant kingdom. *Science Signaling*. 2016, 9.

[2] Maruta, N., Trusov, Y., Brenya, E., Parekh, U., Botella, J.R. Membrane-Localized Extra-Large G Proteins and $G\beta\gamma$ of the Heterotrimeric G Proteins Form Functional Complexes Engaged in Plant Immunity in *Arabidopsis*. *Plant Physiol*. 2015, 167, 1004-16.

[3] Chakravorty, D., Trusov, Y., Zhang, W., Acharya, B.R., Sheahan, M.B., McCurdy, D.W., et al. An atypical heterotrimeric G-protein γ -subunit is involved in guard cell K^+ -channel regulation and morphological development in *Arabidopsis thaliana*. *Plant Journal*. 2011, 67, 840-51.

[4] Botella, J.R. Can heterotrimeric G-proteins help to feed the world? *Trends in Plant Science*. 2012, 17, 563-8.

[5] Maruta, N., Trusov, Y., Chakravorty, D., Urano, D., Assmann, S., Botella, J.R. Nucleotide exchange-dependent and nucleotide exchange-independent functions of plant heterotrimeric GTP-binding proteins. *Science Signaling* 2019, 12.