Consiglio Nazionale delle Ricerche

ISTITUTO PER L'ENDOCRINOLOGIA
E L'ONCOLOGIA SPERIMENTALE
"G. SALVATORE"
2nd UNIT

Seminar

8th November 2023, 14:30h CEST

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TANGO1: from collagen secretion to controlling fibrosis

Host: Alberto Luini (a.luini@ieos.cnr.it)

Conference Room, CNR, P. Castellino Campus

Abstract

Secreted collagens compose 25% of our dry protein weight and necessary for tissue organization, and skin and bone formation. But how are these bulky cargoes that are too big to fit into a conventional COPII vesicle exported from the ER? Our discovery of TANGO1 (Bard, Nature 2006; Saito, Cell 2009; Saito, Mol Biol Cell 2011; Santos, J Cell Biol 2016; Malhotra, Ann Rev Cell Dev Biol 2019), a ubiquitously expressed, ER-exit-site-resident, transmembrane protein has made the pathway of collagen secretion amenable to molecular analysis. TANGO1 acts as a scaffold to connect collagens in the lumen to COPII coats on the cytoplasmic side of ER. However, the growth of the collagen containing mega transport carrier is not simply by accretion of a larger COPII coated patch of ER membrane, but instead by rapid addition of premade ERGIC 53 containing small vesicles and tubules. This mode of transport carrier formation is fundamentally different from that used to produce small COPII vesicles. We have seen that TANGO1 rings the ER exit site and thus organizes a sub compartment within the ER (Nogueira, eLife 2014; Santos, eLife 2015; Raote, J Cell Biol 2017). The transmembrane helices of TANGO1 in prevent the mixing of ERGIC 53 containing membranes to the bulk of ER (Raote et al., 2020). This allows transport of collagen from the lumen of ER into the ERGIC 53 compartment via a tunnel. We have now mapped all the components that work in concert along with the cargo to assemble TANGO1 into a ring (Raote et al., 2018: Raote and Malhotra 2019; Raote et al., 2020 Raote and Malhotra, 2021; Raote et al., 2022). TANGO1 is genetically mutated in patients with collagenopathies (Lekszas et al., 2020). Our ongoing studies on TANGO1 function in exporting right quantity and quality of collagens and how this activity can be targeted to control collagen hyper secretion dependent tissue fibrosis will be discussed.

Biosketch:

VM is ICREA Research Professor and Group Leader and also Coordinator of the Cell & Developmental Biology Program at CRG, Barcelona. He got his D.Phil from Oxford University and then did his post-doctoral studies at Stanford University in the laboratory of the Noble Laureate Jim Rothman. He then moved to UCSD and then to CRG, Barcelona. The discoveries originating from his laboratory include - the identification of Golgi checkpoint in mitosis, the contribution of PKD in regulating membrane traffic out of the Golgi, molecular mechanisms of unconventional secretion and the discovery of TANGO1 a key regulator of collagen trafficking. These discoveries have resulted in more than 100 peer-reviewed publicaitons. He has received several ERC grants and is an elected fellow of EMBO and ASCB. He has served as an Editorial board member of several prestigious journals Cell, JCB, Elife and Molecular Biology of the Cell. More than 25 alumni trained in his lab have become researchers in prestigious universities and institutes.