連絡先；京大病院高齢者医療ユニット、地域ネットワーク医療部

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Cellular senescence is activated in response to developmental signals or stresses during life. It is characterized by a stable proliferation arrest and the acquisition of a senescence-associated secretory phenotype or SASP, composed of numerous factors including pro-inflammatory molecules, proteases and growth factors. Senescent cells can exert beneficial effects when timely regulated (e.g. embryonic development, wound healing) but become deleterious when they accumulate, especially during aging and deleterious exposure (e.g. tobacco, some diets, radiations). The SASP affects the environment of senescent cells by inducing and modulating various phenotypes such as paracrine senescence, immune cell activity, and extracellular matrix deposition and organization, critically impacting various pathophysiological situations, including inflammation, cancer and aging.

We have contributed to the discovery of the important functional roles in regulating cellular senescence of some ions and/or some ion channels in the last years (ref 1-6). In particular, we have identified ITPR2 (Inositol 1,4,5-Trisphosphate Receptor Type 2 or IP3R2) ER-calcium release channel and subsequent mitochondrial calcium accumulation as an important mechanism promoting cellular senescence. Strikingly, *Itpr2* KO mice display lower level of senescence, less marks of aging and they live longer in normal aging conditions. ITPR2 channel also facilitate ER-mitochondria calcium transfer by promoting contacts between these two organelles. I will discuss these published results together with some unpublished results on that topic. I will also share unpublished results supporting a critical role of ANGPTL4 secreted factor as a pioneer SASP component, its mechanism of regulation as well as its function in the SASP to promote inflammation and tumor initiation.

*1 Lallet-Daher H et al, Cancer Res 2013 73:5253-65; 2 Wiel C et al, Nat Commun 2014 5:3792 ; 3 Warnier M et al, Aging Cell 2018 17:e12736; 4 Ma X et al, Aging Cell 2018 17:e12831; 5 Ziegler DV et al, Nat Commun 2021 12:720; 6 Czarnecka-Herok J et al, Redox Biol 2024 73:103204.*

**京都大学医学部附属病院　第一臨床講堂にて**

**令和6年7月22日(月曜)　午後5時30分より**

**Dr. David Bernard**

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**老化セミナー**

**“Deciphering novel mechanisms contributing to cellular senescence and highlighting potential targets against cancer and aging”**