

SEMINAR

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Hosted by Assoc Prof Liou Yih-Cherng

Mechanical force stress regulates tumor immunity

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About the Speaker

Dr. Lanfen Chen is currently a professor at the School of Life Sciences, Xiamen University. She obtained her BS degree at Xiamen University and Ph.D degree at the Albert Einstein College of Medicine, US. She was a Research Fellow at the Brigham and Women's Hospital, Harvard Medical School, Boston, US (2007-2012). She was awarded Chinese National Science Fund for Distinguished Young Scholars and the 17th China Young Women Scientists Awards. Dr. Chen's research group is dedicated to the study of the regulation and physiologic functions of the Hippo pathway in host immune defense, autoimmune diseases, tumor immunity and tumorigenesis, and has published several papers in professional journals such as Cell, Nature Immunology, Cancer Cell, Nature Communications, and so on.

The alteration in extracellular matrix (ECM) architecture and stiffness becomes one of the hallmarks of cancer. We found that the transcription factor Osr2 integrates biomechanical signaling and facilitates the terminal exhaustion of tumor reactive CD8⁺ T cells. Osr2 expression is selectively induced in the terminally exhausted tumor specific CD8⁺ T cell subset by coupled TCR signaling and biomechanical stress mediated by the Piezo1/Calcium/CREB axis. Consistently, depletion of Osr2 alleviates the exhaustion of tumor-specific CD8⁺ T cells or CAR-T cells, whereas forced Osr2 expression aggravates their exhaustion in solid tumor models. Mechanistically, Osr2 recruits HDAC3 to rewire the epigenetic program for suppressing cytotoxic genes expression and promoting CD8⁺ T cell exhaustion. Thus, our results unravel Osr2 functions as a biomechanical checkpoint to exacerbate CD8⁺ T cell exhaustion and could be targeted to potentiate cancer immunotherapy.