

ES cell-derived factors regulate T cell polarization and block DC maturation

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Embryonic stem cells (ESCs) possess immune privileged properties and have the capacity to modulate immune activation. However, the mechanisms by which ESCs inhibit immune activation remain mostly unknown. We recently revealed that human ESC-derived factors block dendritic cell maturation, thereby indirectly affecting T cell activation. We further demonstrated that ESC-derived factors also directly affect T cell activation. ESC-derived factors significantly down-regulated the expressions of IL-2 and IFN- γ , while markedly up-regulating the expression of IL-10, TGF- β , and Treg Foxp3 in CD4+CD25+ T cells. Furthermore, ESC-derived factors robustly suppressed T cell proliferation in response to the protein kinase C- θ (PKC- θ) activator PMA. Moreover, I κ B- α degradation was abrogated, confirming absence of PKC- θ activity. The impact of ESC-derived factors on PKC- θ activation appeared to be specific since other upstream T cell signaling components were not affected. In conclusion, we provide the first evidence that ESCs appear to directly impact T cell activation and polarization by suppressing the PKC- θ pathway without affecting upstream signaling components originating from CD3 and CD28 receptors. Moreover, ESC-derived factors work synergistically with very low dose of immunosuppressive drug cyclosporine (calcineurin inhibitor) to markedly suppress T cell proliferation in response to allo-antigen. Hence, ESC-derived factors may hold the potential to be used as a therapeutic, instead of live ESCs, in overcoming aberrant immune responses. Given the importance of ESC-derived factors in immunomodulation, our current focus has been to identify specific factors that mediate such effects. Accordingly, we have developed a novel proteomic platform and special methodologies.

Biography

Lisheng Wang is currently an Associate Professor in the Department of Biochemistry, Microbiology, and Immunology at University of Ottawa, a Core Member at the Ottawa Institute of Systems Biology, and an Affiliated Investigator at the Ottawa Health Research Institute. Wang has published 52 papers in high profile journals. The average SCI citation of each paper he published is 38. Wang also serves as an editorial board member of repute. He has received 12 awards, including the prestigious New Investigator Award and Maud Menten New Principal Investigator Finalist Prize from Canadian Institutes of Health Research.

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