

DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO

Proposta di progetto per Dottorato

Titolo della ricerca: New strategies to rejuvenate immunity

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Summary della ricerca (fino 300 parole max)

Recent discoveries in Dr. Lanna's laboratory regarding part of the cellular and molecular mechanisms in the field of immunosenescence have led us to focus on how we can harness this knowledge to rejuvenate the immune system and make it more efficient even in the face of the most glaring coronavirus pandemic of the past two years.

Lanna et al. showed that disruption of sMAC (MAP-kinase-bound sestrin stress molecules) by genetic inhibition of sestrins restores immunity during aging. We are trying to improve and develop new compounds able to disrupt sMAC complex and thus revert immunosenescence. On the other hand, the same lab has been discovering the phenomenon of intercellular telomere transfer from APC to T cell during immune synapse that seems to be defective in autoimmune diseases like Multiple sclerosis related to premature aging. TEV (extravesicles containing telomeres) can be harnessed as a new tool to rejuvenate the immune system.

Pertinent Publications of the proponent (last 5 years)

Vaz B, Vuotto C, Valvo S, D'Ambra C, Esposito FM, Chiurchiù V, Devine O, Sanchez M, Borsellino G, Gilroy D, Akbar AN, Dustin ML, Karin M and Lanna A*. Intercellular Telomere Transfer Extends T Cell Lifespan'. *Corresponding (senior) author. Preprint. biorXiv doi: <https://doi.org/10.1101/2020.10.09.331918>

Pereira B, {...} Lanna A{...} Akbar AN*. Sestrins induce natural killer function in senescent-like CD8 + T cells. Nat Immunol. 2020 Jun;21(6):684-694. doi: 10.1038/s41590-020-0643-3

Lanna A*, Gomes DC, Durovic B, McDonnell T, Escors D, Gilroy DW, Lee JH, Karin M & Akbar AN*. A Sestrin-dependent Erk/Jnk/p38 MAPK activation complex inhibits immunity during ageing'. *Co-corresponding author. Nat Immunol. 2017 Mar;18(3):354-363. doi: 10.1038/ni.3665.

Lanna A.' Tuning Telomerase Activity In Senescent Human T Cells Upon Genetic Modification. Methods Mol Biol. 2017;1514:119-126. doi: 10.1007/978-1-4939-6548-9_10

Durovic B*. Lanna A*, Covre L, Henson SM & Akbar AN. 'Killer cell receptor G1 inhibits NK cell function through activation of AMPK. '*Co-First Authorship. J Immunol. 2016 Oct 1;197(7):2891-2899. doi: 10.4049/jimmunol.1600590

Akbar AN, Henson SM & Lanna A* 'Senescence of T Cells: Implications for Enhancing

Human Immunity. *Senior Authorship. Trends Immunol. 2016 Dec;37(12):866-876. doi: 10.1016/j.it.2016.09.002

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- Lanna A, Henson SM, Escors D, Akbar AN. The kinase p38 activated by the metabolic regulator AMPK and scaffold TAB1 drives the senescence of human T cells. Nat Immunol. 2014 Oct;15(10):965-72. doi: 10.1038/ni.2981.

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L. Qin, X. Jing, Z. Qiu et al., "Aging of immune system: immune signature from peripheral blood lymphocyte subsets in 1068 healthy adults," *Aging*, vol. 8, no. 5, pp. 848–859, 2016.

Vicente R, Mausset-Bonnefont A-L, Jorgensen C, Louis-Plence P, Brondello J-M. Cellular senescence impact on immune cell fate and function. *Aging Cell*. 2016;15:400–6

Chou JP, Effros RB. T cell replicative senescence in human aging. *Curr Pharm Des*. 2013;19:1680–98

Bernadotte A, Mikhelson VM, Spivak IM. Markers of cellular senescence. Telomere shortening as a marker of cellular senescence. *Aging*. 2016;8:3–11.

Yu S, Li A, Liu Q, Li T, Yuan X, Han X, Wu K. Chimeric antigen receptor T cells: a novel therapy for solid tumors. *J Hematol Oncol*. 2017;10(1):78

