From immunogenetic polymorphism to functional antitumor lymphocyte mitochondrial dynamics

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- Unlabeled/Unapproved Uses Disclosure: This presentation includes discussion of cell therapies that have not received a clinical indication and should be considered as unlabeled and unapproved clinical use.



Control of self-Ag P1A⁺ tumors by TCRP1A T cells



Pre-tumor vs post-tumor CD8 T cell transfers





T cells and NK cells accumulate in P1A⁺ Tumor



P1A⁺ TIL NK cells show activated phenotype

Which lymphocytes reject Ag-escape tumor variants?





NK cells reject Ag⁻ tumors



- NK cell activation requires T cell help but not vice versa

- NK exhibit activation at the site of ongoing T cell response

Relapse-free survival of breast cancer patients is associated with NK cell activation



Ascierto...Shanker, Marincola, Manjili, J Transl Med, 2013

Mechanisms of intratumoral lymphocyte crosstalk

Roman Uzhachenko, MD PhD





Single contacts between naïve CD8⁺ T (Green DiO) and naïve NK (red DiD) cells



Multiple contacts between activated CD8⁺ T (green) and naïve NK (red) cells

Activated CD8⁺ T cells make physical contacts with NK cells



3D Cultures

Silica nanoneedle 3D matrix provided by Bill Hofmeister, UTSI, Tullahoma, TN

Functional modulation during T-NK crosstalk



Distribution of Memory T cells following T-NK crosstalk



MitoCa²⁺ oscillations during T-NK crosstalk



MitoCa²⁺ staining



Cross-regulatory T/NK mitoCa²⁺



Before contact

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After contact



MitoCa²⁺ oscillations require T-NK physical crosstalk



Blocking LFA1, FasL, NKG2D and cholesterol depletion (lipid raft sequestration)

Signaling cross-talk





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