Not just a protein machine: how ribosomes regulate immune response

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Stellingen behorende bij het proefschrift getiteld Not just a protein machine: How ribosomes regulate immune response.

1. Immune cytokines regulate ribosomal protein composition (this thesis)

2. P-stalk-containing ribosomes preferentially translate mRNAs important for immunosurveillance (this thesis)

3. Loss of ribosomal protein uL14 in tumor cells alters the presented peptide pool (this thesis)

4. Ribosome alterations regulate tumor visibility to $CD8^+$ T cells (this thesis)

5. Ribosome specialization is an emerging field with wide implications (Genuth, N.R. and M. Barna, *The Discovery of Ribosome Heterogeneity and Its Implications for Gene Regulation and Organismal Life.* Mol Cell, 2018. **71**(3): p. 364-374.)

6. Half of the established hallmarks of cancer are regulated by ribosome specialization (Ramalho, S., A. Dopler, and W.J. Faller, *Ribosome specialization in cancer: a spotlight on ribosomal proteins.* NAR Cancer, 2024. **6**(3): p. zcae029.)

7. 'Immunoribosomes' preferentially synthesize peptides for immunosurveillance (Wei, J., et al., *Ribosomal Proteins Regulate MHC Class I Peptide Generation for Immunosurveillance*. Mol Cell, 2019. **73**(6): p. 1162-1173 e5.)

8. Reduced tumor visibility to immune cells is an accepted mechanisms of cancer immune evasion (Blank, C.U., et al., *CANCER IMMUNOLOGY. The "cancer immunogram".* Science, 2016. **352**(6286): p. 658-60.).

9. Cancer cells are under constant selection by the immune system. The ones that survive are the ones that are most responsive to change (Savy, T., et al., *Cancer evolution: from Darwin to the Extended Evolutionary Synthesis.* Trends Cancer, 2025. **11**(3): p. 204-215. Charles Darwin, *The origin of species by means of natural selection, or the preservation of favoured races in the struggle for life*. 1959.)

10. Science has many "dirty little secrets". While the origin of life or dark matter count to the biggest unknowns in science, the antigen processing and presentation (APP) machinery too contains many "known unknowns". Downregulation of APP can make tumor cells invisible to immune cells and it will be essential to develop therapeutic strategies to restore this pathway and sensitize tumors to treatment (Yewdell, J.W., *The seven dirty little secrets of major histocompatibility complex class I antigen processing.* Immunol Rev, 2005. **207**: p. 8-18.; Vyas, J.M., A.G. Van der Veen, and H.L. Ploegh, *The known unknowns of antigen processing and presentation.* Nat Rev Immunol, 2008. **8**(8): p. 607-18.; Blank, C.U., et al., *CANCER IMMUNOLOGY. The "cancer immunogram".* Science, 2016. **352**(6286): p. 658-60.)