Molecular oncology

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Nucleic acid sensing in cancer and infectious diseases

Nucleic acid sensing plays a fundamental role in the maintenance of homeostatic mechanisms at both cellular and organismal levels. Deregulated pathways of nucleic acid sensing contribute to several disorders, including autoimmunity, cancer and infectious diseases. Accordingly, pharmacological intervention on nucleic acid sensing may result in therapeutic effects over a wide range of diseases. Activation of nucleic acid sensing mechanisms triggers innate immunity mechanisms and immunogenic cell death, also promoting adaptive immune responses. Thus, impairments in nucleic acid sensing may alter thresholds for activation of both anti-cancer and antiviral responses. Accordingly, we have demonstrated that viral DNA sensing through the cGAS/STING pathway in tumor cells is crucial for the efficacy of combined treatments with oncolytic viruses and immune checkpoint blockers. The focus of our activity will be dedicated to the analysis of such mechanisms in cancer, as well as in the susceptibility to infectious diseases. Genetic variants of both DNA and RNA sensors will be functionally evaluated in the proposed frameworks.

1. Generation of a Novel Mesothelin-Targeted Oncolytic Herpes Virus and Implemented Strategies for Manufacturing.

Froechlich G, Gentile C, Infante L, Caiazza C, Pagano P, Scatigna S, Cotugno G, D'Alise AM, Lahm A, Scarselli E, Nicosia A, Mallardo M, Sasso E, Zambrano N.Int J Mol Sci. 2021 Jan 6;22(2):477. doi: 10.3390/ijms22020477.PMID: 33418877

 Integrity of the Antiviral STING-mediated DNA Sensing in Tumor Cells Is Required to Sustain the Immunotherapeutic Efficacy of Herpes Simplex Oncolytic Virus.
Froechlich G, Caiazza C, Gentile C, D'Alise AM, De Lucia M, Langone F, Leoni G, Cotugno G, Scisciola V, Nicosia A, Scarselli E, Mallardo M, Sasso E, Zambrano N.Cancers (Basel). 2020 Nov 17;12(11):3407. doi: 10.3390/cancers12113407.PMID: 33213060

3. New viral vectors for infectious diseases and cancer. Sasso E, D'Alise AM, Zambrano N, Scarselli E, Folgori A, Nicosia A.Semin Immunol. 2020 Aug;50:101430. doi: 10.1016/j.smim.2020.101430. Epub 2020 Nov 29.PMID: 33262065

4. Replicative conditioning of Herpes simplex type 1 virus by Survivin promoter, combined to ERBB2 retargeting, improves tumour cell-restricted oncolysis.

Sasso E, Froechlich G, Cotugno G, D'Alise AM, Gentile C, Bignone V, De Lucia M, Petrovic B, Campadelli-Fiume G, Scarselli E, Nicosia A, Zambrano N.Sci Rep. 2020 Mar 9;10(1):4307. doi: 10.1038/s41598-020-61275-w.PMID: 32152425

5. A long non-coding SINEUP RNA boosts semi-stable production of fully human monoclonal antibodies in HEK293E cells.

Sasso E, Latino D, Froechlich G, Succoio M, Passariello M, De Lorenzo C, Nicosia A, Zambrano N.MAbs. 2018 Jul;10(5):730-737. doi: 10.1080/19420862.2018.1463945. Epub 2018 May 10.PMID: 29658818