Cancer-related changes in human non-tumorigenic lung epithelial cells exposed to alpha radiation in combination with nicotine

Nadia Boroumand[1], Karine Elihn[2], Andrzej Wojcik[1], Lovisa Lundholm[1]

[1]Centre for Radiation Protection Research, Department of Molecular Biosciences, The Wenner-Gren Institute, Stockholm University, Sweden

[2]Department of Environmental Science, Stockholm University, Sweden

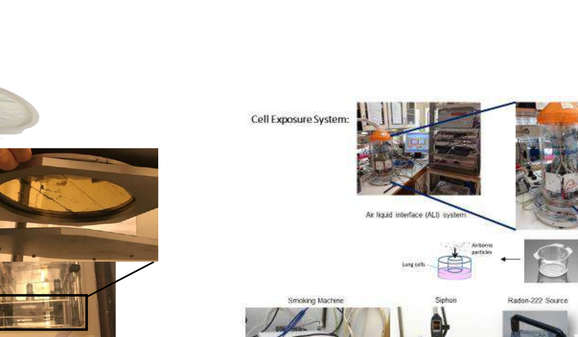
*Correspondence: nadia.boroumand@su.se

Introduction and methods:

The carcinogenic effect of radon - the second largest cause of lung cancer - has encouraged the European Commission to fund the RadoNorm project. One of its aims is to reduce uncertainties in radiation risk management by assessing biological mechanisms underlying radon interaction with other stressors such as smoking. The first sub-project is focusing on the interaction between nicotine and alpha particles in inducing lung cancer from which some preliminary data are presented here. Bronchial epithelial BEAS2B cells were pretreated with 2 µM nicotine for 16 h and then given 1 Gy alpha particles. The main project will evaluate the effect of radon alone and in combination with other stressors including smoking and nanoparticles in lung cancer development using a range of cytogenetic and molecular endpoints.

Cancer-related changes in cells exposed to alpha radiation from radon in combination with airborne particles

- Molecular mechanisms of radon-induced lung cancer
- Combination with other stressors



- How it affects radon risk level?
- Molecular mechanisms and patterns of interaction with radon

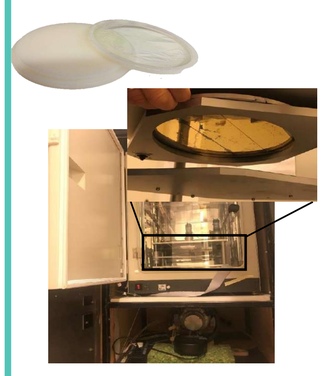
- Any interaction with smoking and radon in inducing lung cancer?

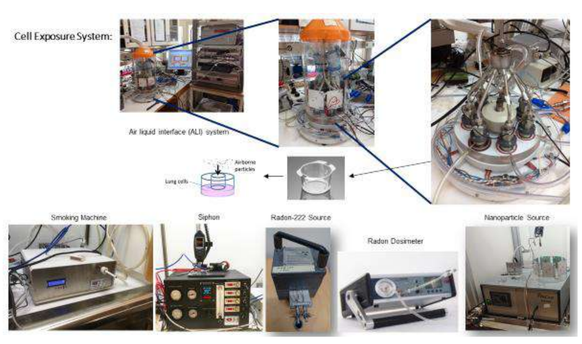
2021-2022 — 1

- Nicotine
- Alpha Particle
- Hormones

2022-2025 — 2

- Smoking
- Radon
- Other Stressors

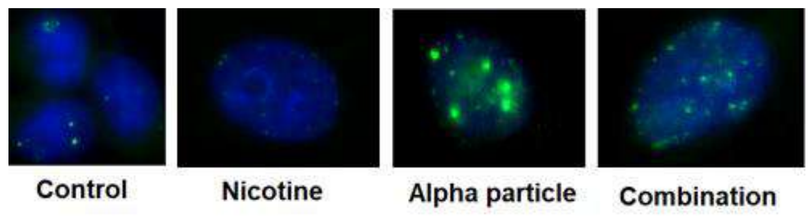




Within 24h — At 24h — Within a window of 4-13 days

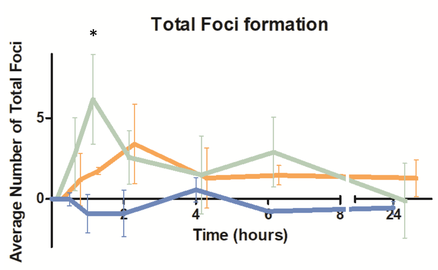
Gamma H2AX — Cell counting and reseeding — MTT and Clonogenic Survival

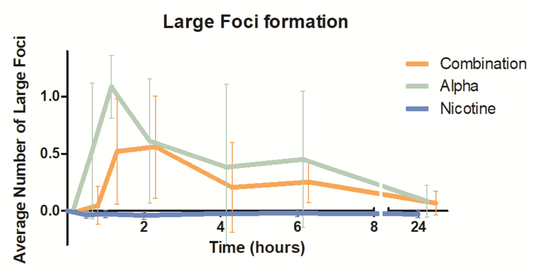
γH2AX assay:

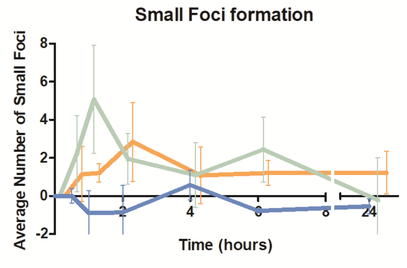


Optimized conditions for the rest of the study:

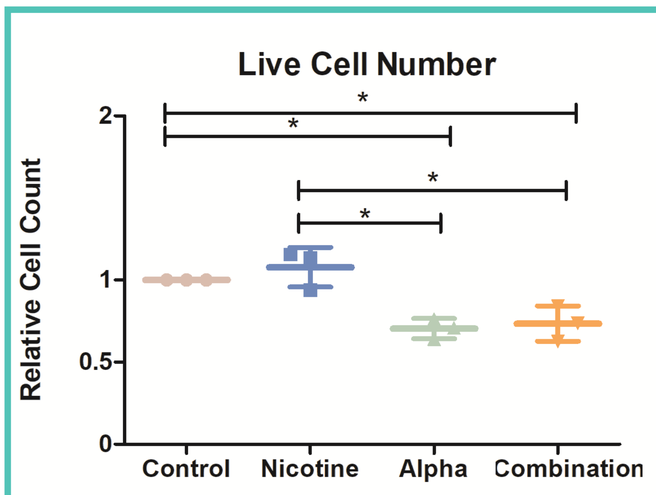
- Nicotine 2uM
- Alpha Particle 1 Gy

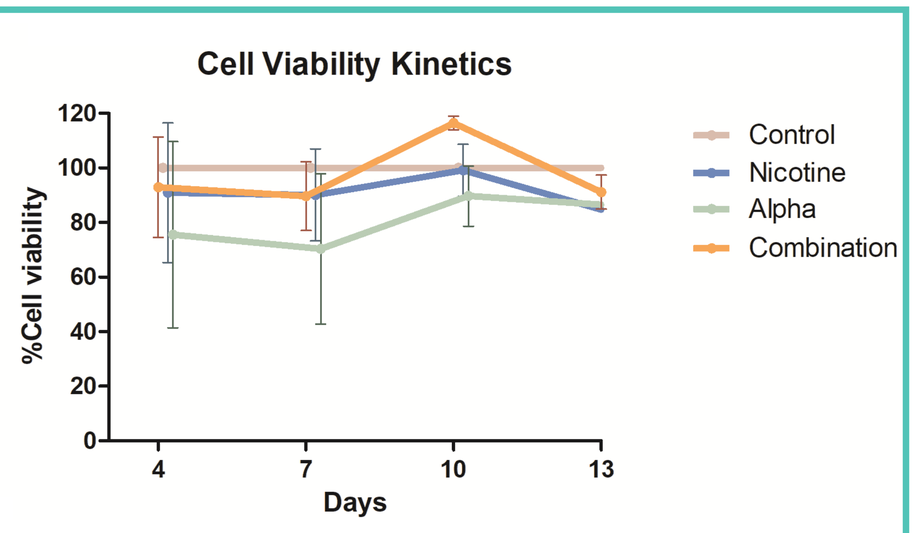


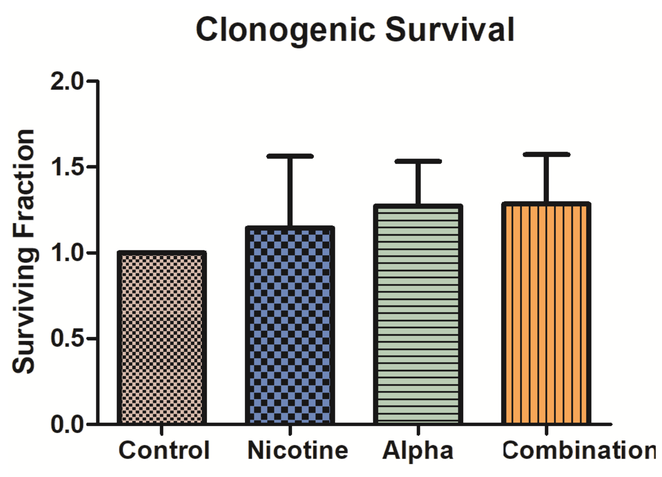


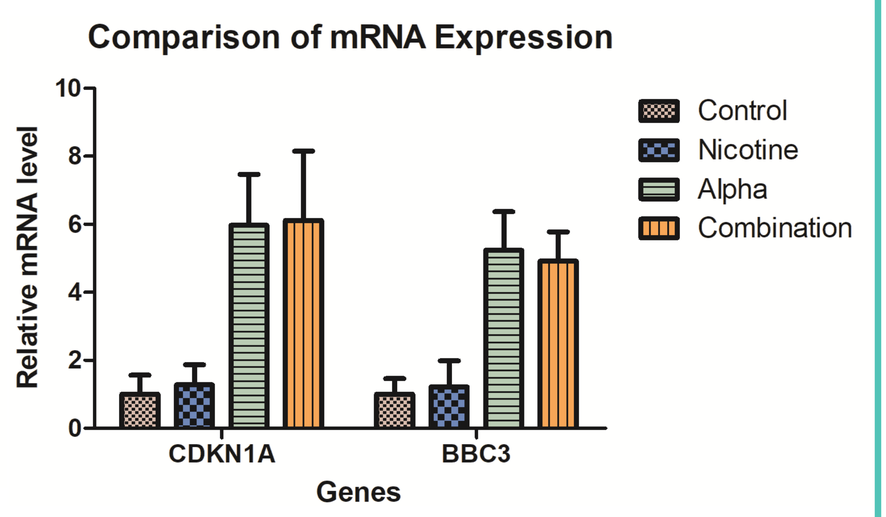


*Asterisks represent significant difference at the level of <0.05 between the Alpha and Combination group.



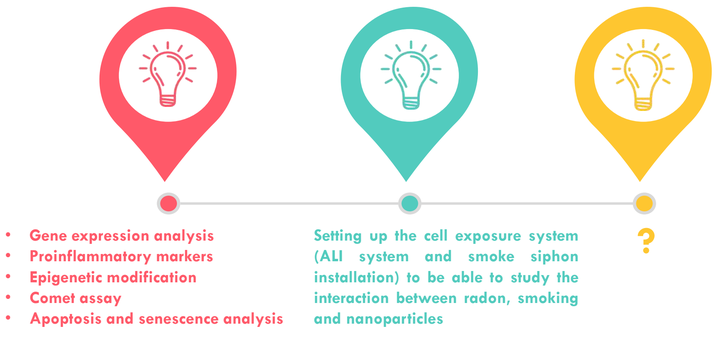






*Asterisks represent significant difference at the level of <0.05.

Upcomings:



Conclusion:

The results showed that alpha particle exposure induce complex damages which lead to cell death, however, nicotine can affect the cell response to alpha particle irradiation. Particularly at the level of gamma-H2AX foci the result indicated the formation of large foci in alpha particle-irradiated cells, confirming the formation of more complex damage, while nicotine-treated cells did not induce any prominent number of foci. The repair kinetic curve showed a biphasic response in response to alpha particles with peaks after 1 h and 6 h, whereas the combined exposure produced a delayed, flattened response, where more foci remained unrepaired after 24 hours. Nevertheless, mRNA expression of radiation-induced p53-target genes CDKN1A, mediating cell cycle arrest, and BBC3, promoting apoptosis, was increased after alpha radiation exposure, but similarly with or without nicotine. Further analysis are required to shed a light on the interaction between these two factors in inducing lung cancer.

References:

1.Takano, M., et al., Nicotine transport in lung and non-lung epithelial cells. Life Sci, 2017. 188: p. 76-82.

2.Lee, H.W., et al., E-cigarette smoke damages DNA and reduces repair activity in mouse lung, heart, and bladder as well as in human lung and bladder cells. Proc Natl Acad Sci U S A, 2018. 115(7): p. E1560-E1569.

www. Radonorm.eu

This project has received funding from the Euratom research and training programme 2019-2020 under grant agreement No 900009.