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Biological effects of exposure to hydrothermal gas in cell models of the bronchi

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**Summary of the project:**

This PhD project will study the primary response of human bronchi upon aggression by gaseous volcanic gas. It will be focused on the case of Soufriere de Guadeloupe volcano, which produces vast amounts of H2S, a common volcanic hydrothermal gas, impacting the communities downhill of the volcano. The project will provide dose-response curves of various biological endpoints for healthy vs. asthmatic bronchial cell models in different exposure scenarios, and will lead to identifying biomarkers of bronchi injury triggered by exposure to hydrothermal gases. We will conduct a series of experiments using a sophisticated *in vitro* approach with well-established cellular models of the human conductive airways (bronchial epithelium) to evaluate the ability of H2S to induce common injury responses, including cytotoxicity, oxidative stress and (pro-)inflammatory response (release of cytokines involved in the sterile inflammation of the bronchi), in healthy and asthmatic cells. A range of concentrations (from 1 to 200 ppm, representing the range of H2S measured from the summit downhill) and exposure durations (half an hour up to weeks to represent acute and sub-chronic scenarios) will be tested on cells cultured at the air-liquid interface (ALI). The experiments will be run using a sophisticated multi-cellular model of bronchial epithelium cultured at the ALI (MucilAirTM) which consists of primary bronchial epithelial cells, including basal, ciliated, and mucus-producing cells, therefore possessing the active protective mechanism of in vivo lung conditions. The model is composed of cells derived from healthy or asthmatic donors, is readily available from the supplier (Epithelix SAS, France) and allows long-term repeat-dose toxicity testing (up to 5 weeks).

To administer gas to the cells, we will use the innovative cell exposure system Celtox sampler. In this system, within a sealed air-tight chamber, cell-culture plates can be exposed to a precisely controlled concentration of gas using a continuous gas flow system operated at 2 L/min. This system allows gas injection in a heated, atmosphere-controlled enclosure, using gas bottle standards of known H2S concentrations (Messer, France; bottles with standard concentration at 1, 10, 100, 200 ppm), or natural volcanic gas samples from Guadeloupe (Multi-layer foil gas sampling bags sampled to expose to the full gas cocktail of hydrothermal emissions). Cell responses will be assessed following exposures for cytotoxicity (LDH release, CCK8 assay), oxidative stress (expression of related genes e.g. HMOX1, NQO, SOD2, CATm, NFE2L2, Gpx31 assessed by RT-qPCR and confirmed by proteins assays) and (pro-inflammatory response related to non-allergic asthma (interleukin-6, 8, 17, 23, 25, 33 and thymic stromal lymphopoietin59 assessed by multiplex immunoassays platforms - Mesoscale and Luminex- already used on site).

These experiments, conducted by the recruited PhD student, will provide insight into the potential for exposure to volcanic degassing to exacerbate preexisting bronchial respiratory diseases and reveal whether the effects of persistent exposure are more adverse than acute exposure, in both asthmatic and healthy cells. They will also allow identifying molecules produced by the cells following exposure to hydrothermal gases in the different scenarii tested, that can be dosed in the blood and/or bronchoalveolar lavage, and used as potential biomarkers to monitor population health in the exposed areas.

**Related recent publications of the team**

[1]. **Eychenne, J.,** Gurioli, L., Damby, D., Belville, C., Schiavi, F., Marceau, G., Szczepaniak, C., Blavignac, C., Laumonier, M., Gardés, E., Le Pennec, J.-L., Nedelec, J.-M., Blanchon, L. and **Sapin, V**., 2022. Spatial distribution and physicochemical properties of respirable volcanic ash from the 16-17 August 2006 Tungurahua eruption (Ecuador), and alveolar epithelium response in-vitro. GeoHealth: e2022GH000680

[2]. Loubet F, Robert C, Leclaire C, Theillière C, Saint-Béat C, Lenga Ma Bonda W, Zhai R, Minet-Quinard R, Belville C, Blanchon L, **Sapin V**, Garnier M, Jabaudon M. Effects of sevoflurane on lung alveolar epithelial wound healing and survival in a sterile in vitro model of acute respiratory distress syndrome. Exp Cell Res. 2024 May 1;438(1):114030. doi: 10.1016/j.yexcr.2024.114030.

[3]. Tomašek I, **Eychenne J**, Damby D.E, Hornby A.J., Romanias M.N., Moune S., Uzu G., Schiavi1 F, Dole M., Gardès E., Laumonier M., Gorce C, Minet-Quinard R., Durif J., Belville B., Traoré O, Blanchon L., **Sapin V**. Physicochemical Properties and Bioreactivity of sub-10 μm Geogenic Particles: Comparison 1 of Volcanic Ash and Desert Dust [submitted for publication in GeoHealth]

**Applications (CV and motivation letter) should be sent to both supervisors by e-mail before November 10, 2024.**