Résumé CORSICA - 2024_RF_013

Effets combinés des RF à 26 GHz et de différentes radiations UV sur la peau et la cornée in vitro

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Projet complet - 36 mois
Budget : 290 134 € TTC

Objectif détaillé

The objective of the CORSICA project is to investigate the in-vitro effects on human skin and eyes of the co-exposure between 5G modulated - radiofrequency fields (RF) at 26 GHz (at absorbed Power Density levels up to 10 W/m2) and ultraviolet (UV) radiations at different wavelengths (UV-A, UV-B, and solar)

(i) To assess the effects of a 26 GHz, 5G modulated signal alone or in combination with UV radiation on viability, reactive oxygen species (ROS) production and inflammation in skin and eye models

(ii) To assess the effects of a 26 GHz, 5G modulated signal alone or in combination with UV radiation on genotoxicity in 2D-3D skin models

(iii) To assess the effects of a 26 GHz, 5G modulated signal alone or in combination with UV radiation on irritation and muscin production (dryness) in cornea models

Originalité et/ou caractère novateur du projet

Over the past few decades, mobile telephony has experienced rapid deployment, with the introduction of the fifth generation (5G) beginning in 2020. In Europe, the initial frequency range selected for the introduction of 5G falls between 3.4 and 3.8 GHz. However, in the coming five years, the 26 GHz band, for which limited studies have been published, is scheduled for deployment.

The originality of the CORSICA project is to investigate, in vitro, the possible effects of a 5G signal at 26 GHz on the two main biological, superficial targets at such frequencies, that is the skin and in the eye, the cornea.

Moreover, there are few investigations of the effects of RF in combination with other exposures, and such studies do almost not exist using RF at 26 GHz. CORSICA will investigate the effects of a concurrent exposure of the human skin and cornea to RF and either solar, UV-B or UV-A radiations, also a routine occurrence in the daily life.

We find it very pertinent to study the possible interaction between RF exposure classified as a possible human carcinogen and UV and solar exposure categorized as a human carcinogen by the International Agency for Research on Cancer. Of note, high doses of UV radiation can have detrimental effects on the skin (burns) and the eye (photokeratitis), with sources including sunlight and artificial sources like UV lamps. Chronic exposures to UV radiation has the potential to inflict damage to the skin leading to tumor formation, as well as to the eye leading to cataract, and possibly to syndrome of Age-Related Macular Degeneration.

Questions de recherche

RFES 1.1 - Études in vitro, in vivo ou cliniques sur les mécanismes d'action de l'exposition (aiguë et chronique) du vivant aux radiofréquences, aux niveaux moléculaire et cellulaire, en tenant compte des évolutions d'utilisation de fréquences liées aux nouveaux usages et nouvelles technologies de communication. Les études s'intéressant aux bandes de fréquences nouvellement identifiées (pour la 5G par exemple) et encore peu étudiées (3,5 GHz, 26 GHz et au-delà, notamment) sont prioritaires.

RFES 1.5 - Études sur des modèles in vitro (de la peau, de la cornée, de la conjonctive, ...) de l'exposition aux fréquences supérieures à 10 GHz afin de mesurer des paramètres tels que la viabilité cellulaire et la génotoxicité, par exemple.

RFES 2.3 - Étude des effets des co-expositions aux radiofréquences se rapprochant des situations réelles d'exposition et permettant d'analyser l'effet combiné des radiofréquences et d'autres facteurs environnementaux (physiques ou chimiques) sur l'organisme.

CORSICA mainly aims to answer the questions RFES 1.1, 1.5, and 2.3.

RFES 1.1., RFES 1.5. Using 2D and 3D models of skin and cornea, we aim to evaluate the capacity of 5G RF signals at 26 GHz to participate in oxidative stress, inflammation, and cell death. We will address more biological endpoints in specific models such as genotoxicity for the skin models or mucin production for the cornea models.

RFES 2.3. Of note, 3D models are considered as an alternative for in vivo assays, in agreement with the 3R approach (Replace, Reduce, Refine), and provide models closer to the in vivo situation. CORSICA will investigate whether 26 GHz RF signals could alter the effects of UV radiation on ROS production and inflammatory response in skin and ocular models. To better understand the interaction between the two agents, we will test for different UV radiation (UV-B, UV-A, or solar UV) and for different RF exposure conditions (2 exposure and post-exposure timepoints, 3 RF exposure levels).

Description des méthodes mises en œuvre

The following models will be used :

- 2D skin cell cultures commercial (Lonza and Gibco).
- 3D Skin model will be obtained by Phenion (France).

The effects on viability (MTT), ROS production, inflammatory cytokines secretion (IL-1, IL-6, IL-8, etc by ELISA), epidermal architecture, apoptosis, DNA damage, antioxidant levels, protein oxidation / 8-oxoguanin levels will be followed at different time points post-irradiation. The T4 enzyme modified Comet Assay will be used for the detection of DNA damage including CPDs as the predominant form of DNA damage induced by UV-B.

- 2D cornea cell culture is commercial (ATCC), it is composed by normal human primary corneal epithelial cells.
- 3D models are either reconstructed cornea (Mattek) or cornea organoids. Cornea organoids are obtain from IMR-90.4 iPSC cells maintained by clonal propagation on growth factor-reduced Matrigel® in mTeSR1 medium under hypoxia.

The effects on viability, ROS production (flow cytometry), inflammatory cytokines secretion, antioxidant levels, apoptosis, and protein oxidation (Western blot) will be followed at different time points. Specific tests for mucin secretion (at the protein and gene levels) will be performed on 3D reconstructed cornea.

For all biological endpoints, positive (exposure to UV or chemicals) and negative (Sham-exposure) controls will be provided and data will be obtained on coded samples.

The first 10 months of the project will be devoted to setting all cellular models and their dosimetric characterization at 26 GHz and with the different supports for cell cultures, organoids, and reconstructed tissues. Experiments on the skin and the cornea will be performed in parallel in the two laboratories over the next 26 months, allowing for the exchange of setup or cell models, if needed. Indeed, the CORSICA consortium federates two teams internationally recognized as for their expertise in UV radiation bioeffects and/or in bioelectromagnetics, thus providing synergistic state-of-the-art technical competences. The possibility to exchange exposure setup and the capability to perform combined exposure to UV radiation leads to a strong added value component. The CORSICA research team will thus be composed of 5 researchers, 3 engineers and 2 technicians.

Partner 1: Bioelectronics team of the IMS laboratory - UMR 5218 CNRS (Bordeaux, France): cell culture facility, RF exposure setups, UV irradiator, biological tests, electronics and signal analysis, experimental dosimetry. Specifically, the in vitro 26 GHz exposure setup, a triple reverberation chamber, is currently designed within the RF Skin-UV project. The dosimetric characterization (simulations) of the exposure setup will be subcontracted to XLim (Limoges, France).

Partner 2: National Center for Public Health and Pharmacy (NCPHP), Unit of Non-Ionising Radiation (Budapest, Hungary): cell culture facility, UV irradiators, solar simulator SOL-500. Specifically, the 26 GHz exposure system consists of a horn antenna associated with RF devices in a box covered with an absorbing material.

Partenariat

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