**Contribution aux exercices de prospective 2020-2030**

***Contribution to the 2020-2030 prospective reflection***

**Sciences Nucléaires et Vivant**

*Nuclear Science and Health*

**Description détaillée de la contribution**

*Detailed description of contribution*

***Please indicate science objectives (2 pages max. including figures)***

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**Please send this document to** [PROSP2020-GT10-COPIL-L@IN2P3.FR](mailto:PROSP2020-GT10-COPIL-L@IN2P3.FR) **before   
november 1st, 2019**

Caractérisation, mesure et modélisation des faibles doses et de leur impact sur le stockage de matériaux biologiques au Laboratoire Souterrain de Modane

Modane Underground Laboratory (LSM) is located in the middle of the Fréjus tunnel , this location reduces the muon flux from 107 /m2.day to 4 allowing physicist to built low background experiments. The LSM hosts experiments on different topics ranging from astroparticle to environmental science and low radioactivity measurement. This location was used to measure the impact of cosmic rays and natural radioactivity on stemcells stored at liquid nitrogen temperature. The experiment consisted in the comparison between four cryogenic setups summarized hereafter.

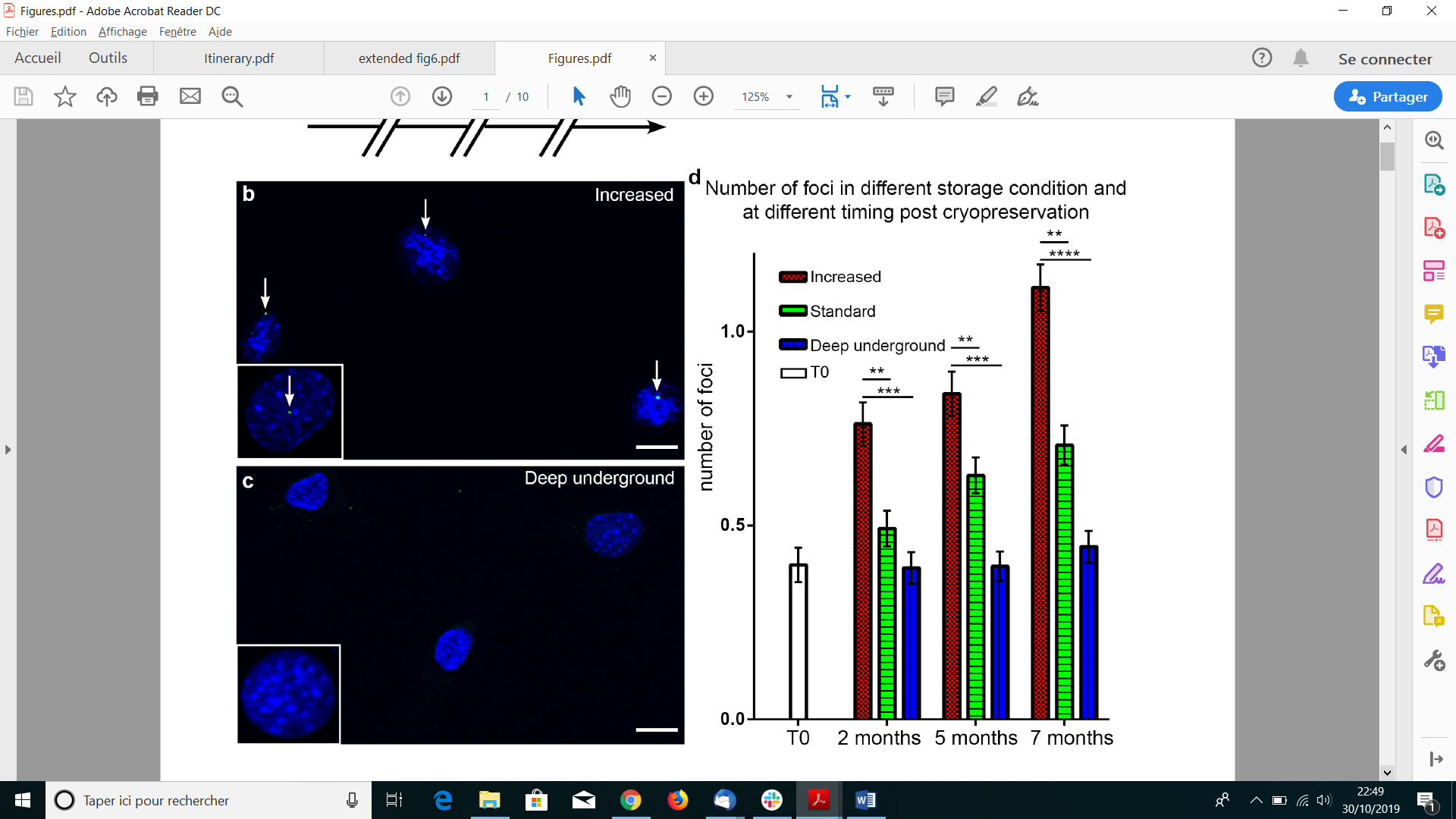
Our reference is the usual storage of the stem cells : a cryostats located in the second basement under a building in the Institut Pasteur. This corresponds to 10 m.w.e shield reducing by a factor 10 the cosmic ray flux compared to a surface storage. This state is called “Condition Reference”.

To increase specifically the cosmic neutron flux by a factor 3 we installed a cryostat at an altitude of 1096m in the LSM surface building. This state is called “Condition Altitude”.

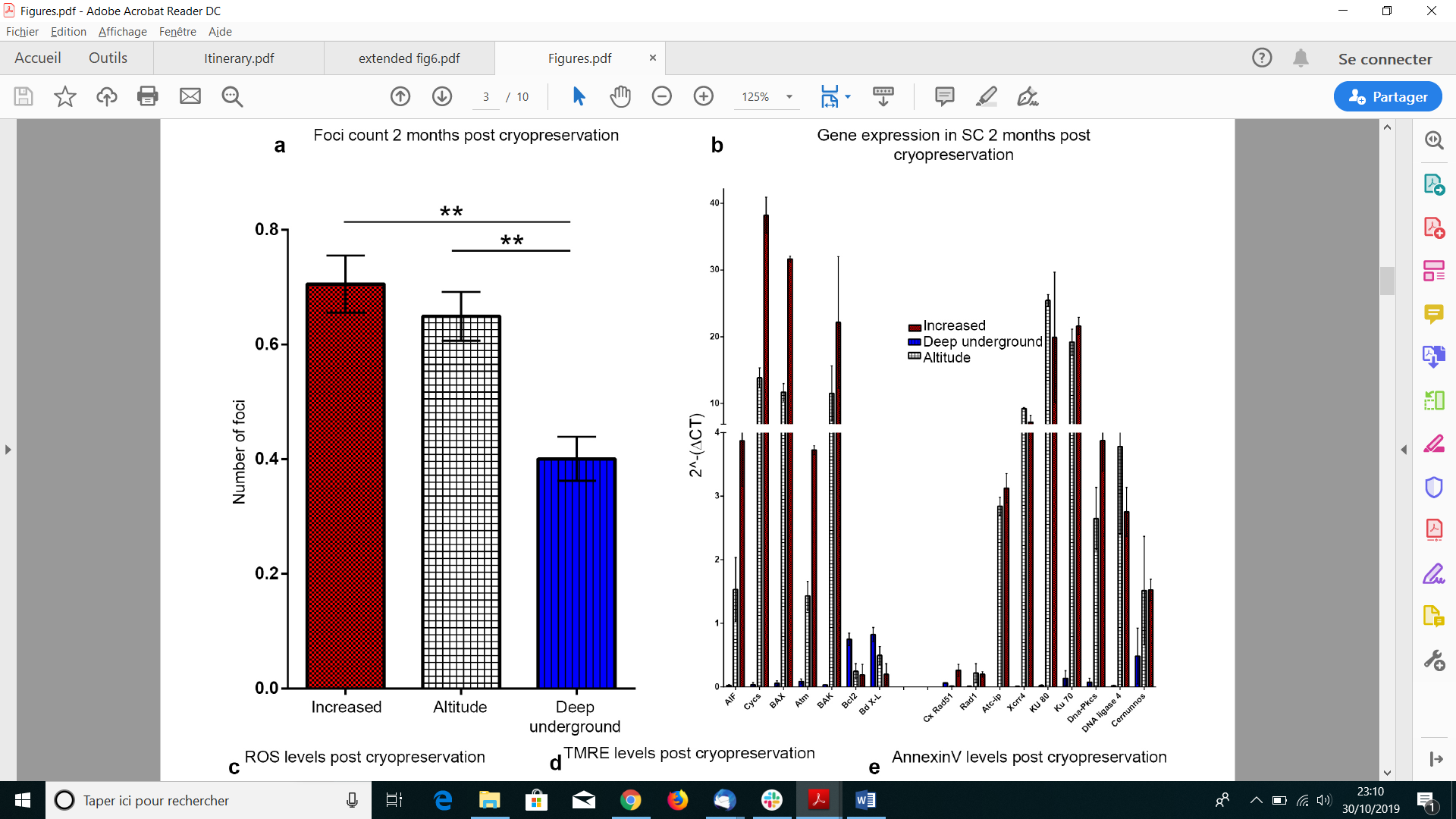
To increase the gamma-ray flux, we placed a sand containing Thorium at the bottom of the cryotubes (Figure 5a). Measure gives a daily dose of 0.21 mSv/day. Two months of exposure to the radioactive gamma-ray source will correspond to 14.6 years in natural ambient radioactivity. The cryostat is also located in altitude (1096m) so cosmic neutron flux will also be increased. This state is called “Condition Increased”.

The suppression of the cosmic neutron is obtained placing a cryostat at 1 700 m (4 800 m.w.e) below the surface. The muons are reduced by a factor 2.5 millions compare to the surface. In fact the cosmic neutrons are negligible at this depth as well as the neutrons from natural radioactivity.

To measure the impact of ionising radiation on the cryostored stemcells we chose to count the foci on nuclear DNA. We compare also different parameter including ROS and gene activities upon thawing.



The number of foci increased as the dosis and the cosmic ray flux increases. Moreover the number of foci increases respect to the time of exposure.



An interesting result was that the cosmic rays produced the same number of foci as an increase of radioactivity.

The conclusion of these experiments are that cosmic rays and natural radioactivity are a threat for the long time cryostorage of stemcells. Other tests made on the cells also show that natural radioactivity is responsible for an increase of reactive oxygen species. Moreover stemcell stored in the shield in LSM showed a better engrafment potential. These observation have been reproduced on three different type of mice stemcells.

To the best of our knowledge it is the first measurement of the action of cosmic ray at the sea level on cryostored samples. These measures lead to a patent on cryostats. Currently an article is under review for Nature Communication.

The following experiment could be reproduced on different samples to measure the impact of cosmic ray on different cells. This is already a solid indication that long term storage must take ionnising radiations into account to be relevant especially for hospital and companies.

Currently we are investigating pine seeds, gamete and oak seeds. We also want to combine these measure with simulation to have a model that would predict the damage measured during preservation. The number of cells stored could be vastly increased since the cryostat that had been built for this research have still room for other samples from different origins. The ideal situation would be to study gametes and seeds from a wide range of species. For examples eggs from fish, birds, reptiles and mamalians. A specific attention must be paid to the regulation of storage of biological material to perform these experiment in an underground laboratory.

The study will need biological partner specialise in analyzing the DNA and other parameter cells to be able to extract the result. Moreover some studies could be conducted over the cell awakening using the biological lab of LSM. The studies could show the interest of cultivating cells without radioactivity, moreover it could be submitted to a controlled low dosis of radioactivity.