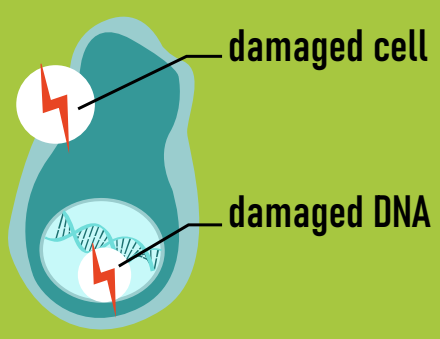
A mutagenic test for nanomaterials (NMs)

ASSESSMENT OF MUTAGENIC RISKS

Nowadays, the mutagenic tests used for chemicals are **poorly adapted to evaluate the potential mutagenicity risk of nanomaterials**.

WHAT IS MUTAGENICITY?

Mutagenic substances:



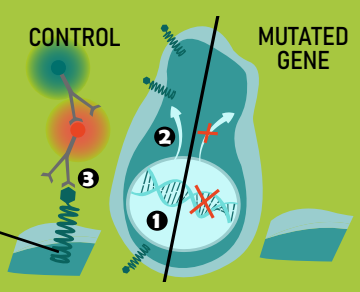
Most of the mutagenic substances are carcinogenic and induce an increased the risk of cancer.

PIG-A, A GENE TO DEVELOP MUTAGENIC TEST

This test should be performed on alveolar macrophages, as they internalize NMs. It focuses on the PIG-A gene which is used as **a reporter of environmental mutagenesis: one PIG-A gene mutation** leads to the **loss of the transmembrane anchor** at the cell surface.

The presence of this anchor can be detected using **fluorescent markers.** Two markers have been used to avoid a misunderstanding caused by a dysfunction of one of them.

1 PIG-A gene codes for a specific protein, **2** which with others participate in the synthesis of a **transmembrane anchor** **3** recognized by markers.



A mutation on this gene **prevents the synthesis of the anchor**. Thus, no markers will be able to detect it.

If the **tested substance is mutagenic,** the studied gene will be mutated and the transmembrane anchor will not be synthetised: **there will not be any fluoresence** compared to control.

OBJECTIVE

Developing a **new mutagenic test** applicable to nanomaterials.

SOME RESULTS OF THE PROJECT

To develop a new mutagenic test for nanomaterials, 2 main steps have to be performed:

- verifying that the test is functional and works with different molecules known to be mutagenic,
- analyzing the mutagenic stress with nanomaterials.

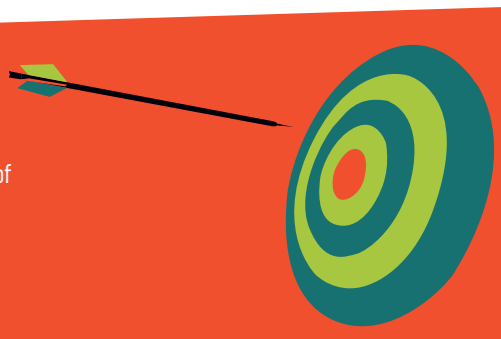
Assessment of the test with two known mutagenic chemicals : etoposide (ETP) and methyl methanesulfonate (MMS)

To analyze the test efficacy, **cells were exposed to mutagenic chemicals (ETP or MMS), or only to the solvent**. After **two days of exposure, the fluorescence have been observed** to analyze the presence of the transmembrane anchor. Cells are represented by green dots.

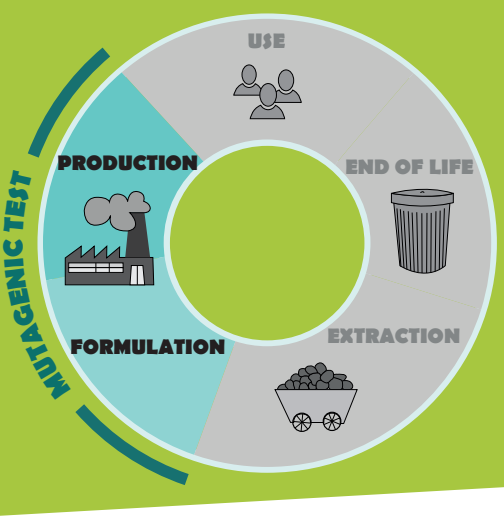
- With the **solvent only**, every cell shows fluorescence, the transmembrane anchor is present for all of them.
- With **a known mutagenic chemical** (etoposide or methyl methanesulfonate), a significant proportion of cell having no fluorescence appears. The absence of fluorescence is explained by the lack of the anchor, due to the mutation of the gene PIG-A.

The mutagenic test PIG-A is able to reveal the mutagenic properties of etoposide and methyl methanesulfonate.

Further experiments have to be performed with others mutagenic molecules to confirm the efficiency of the protocol efficiency, but it is **promising to evaluate the mutagenic risk of nanomaterials**.



LIFE CYCLE STAGES STUDIED



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Serenade
Safe(r) Ecodesign Research and Education applied to ANanomaterial DEvelopment.

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