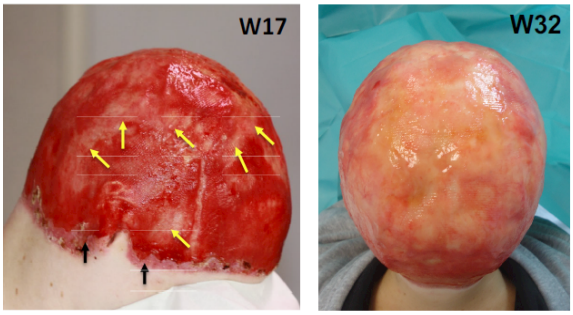
PARTNERING OPPORTUNITY

Repurposing of p53-reactivating compounds for ectodermal dysplasia syndromes (Dr. D. Aberdam, Pr. S. Hadj-Rabia)

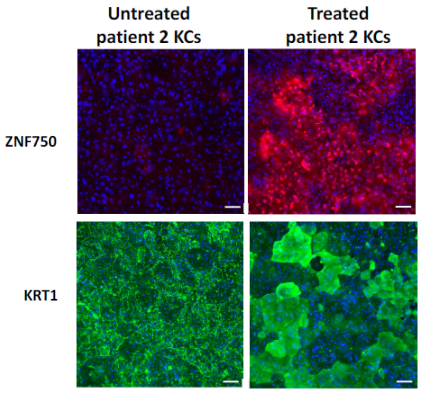
The present project and invention relates to the **repurposing of methylene quinuclidinone to treat AEC and EEC syndromes in inducing a rescued differentiation of epithelial cells**

AEC and EEC syndromes are forms of ectodermal dysplasia, a group of about 150 conditions characterized by abnormal development of ectodermal tissues including the skin, hair, nails, teeth, and sweat glands, caused by loss of function mutations in P63 gene, in domains highly conserved with the P53 gene



Type of project

- Pharmaceutical
- Dermatology
- Repurposing
- Orphan development



Project highlights

- **Primary targets:** skin healing and shortening of skin aplasia in ectodermal dysplasias (1 in 100,000 newborns in the US)
- **Secondary targets:** skin diseases with defective wound healing, such as venous ulcers
- **Repurposing of topical quinuclidinone derivatives**
- **Patent:** Methods and compositions for promoting wound healing in a subject suffering from ectodermal dysplasias (WO/2020/016155 - priority data 16.07.2018)
- **Publication:** Aberdam E et al. Improvement of epidermal covering on AEC patients with severe skin erosions by PRIMA-1MET/APR-246. Cell Death Dis. 2020 Jan 16;11(1):30.

Results & proposed plan

- Quinuclidinone derivatives treatment shows:
  - in vitro: induction of epithelial markers expression in primary keratinocytes derived from AEC patients indicative of differentiation induction
  - Preliminary clinical proof-of-concept: re-epithelialization of skin erosions and a drastic improvement of pain, leading to stop painkillers, in two children treated with quinuclidinone derivatives, with no side toxic effects observed
- Production of GMP-grade compounds
- Clinical trial with additional patients in the frame of the ERN-SKIN network
- Challenging of Quinuclidinone on other rare skin diseases indirectly related to p63

Resources and expertise

- **Integrated Care and Research teams:**
  Dr. Daniel Aberdam (INSERM U976, University of Paris, France)
  Pr. Smail Hadj-Rabia, Pr. Christine Bodemer (INSERM U1163 UMR-S1151, Department of Dermatology and Reference center for Genodermatoses and Rare Skin Diseases (MAGEC) Necker Hospital / Imagine Institute)
- Access to cohort of patients and patients' samples, cell models

CONTACT

Nicolas Doulet Innovation & Technology Transfer Department
+33 (0)1 42 75 43 55
nicolas.doulet@institutimagine.org

IMAGINE Institute. Located on Necker-Enfants malades Hospital campus in Paris, Imagine Carnot Institute's main strength is to bring together, on a single site, 1,000 of the best specialists in genetic diseases, with the ambition to change the lives of families affected by genetic diseases. First European center of research, care and education on genetic diseases, the Imagine Carnot Institute aims to understand them and cure them. Its patient-centered organization and the close collaboration between clinicians and researchers nurture a unique translational model that facilitates research collaborations and the establishment of new therapeutic strategies with industrial partners.

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