Phototrexate

The first light-regulated drug candidate for the treatment of psoriasis and cancer

The Challenge

Severe hyperproliferative diseases of the skin and other tissues (where cells grow without control), such as psoriasis, are often treated with high doses of antiproliferative drugs like methotrexate. They must be administered systemically and cause important off-target toxicity and adverse effects that reduce their therapeutic efficacy and tolerated doses. Alternatively, therapeutic effects can be localized using light to photogenerate cell-killing oxygen species (photodynamic therapy, PDT). **Although the interest in PDT is on the rise in dermatology and oncology (with an expected market growth above 7% until 2022), the lack of pharmacological specificity of PDT photosensitizers and their poor effectiveness in hypoxic tumors has limited their advantages**.

The Technical Solution

To solve this problem, Phototrexate (PHX), a light-regulated, target-specific antiproliferative compound (including a wide range of analogs), has been developed. PHX is based on an antiproliferative drug approved against psoriasis and several cancers. It is designed to be constitutively inactive in its thermodynamically stable configuration, while it can be activated with light to locally provide the specific pharmacological effects of the reference drug.

The Market & Potential Applications

Psoriasis is a chronic immune-mediated skin disorder that affects about **2–3% of the population worldwide**. Plaque psoriasis, the most common form, affects ~80–90% of patients with psoriasis. The global psoriasis market generated revenues worth US$7.49 billion in 2014. The top five products accounted for 82% of the market value. The psoriasis market is projected to reach $9.02 billion by 2019 (with a 2014–2019 compound annual growth rate (CAGR) of 3.8% (IMS Midas, IMS Health).

Moreover, it has potential application in the following Markets:

- Other **chronic inflammatory disorder** such as juvenile dermatomyositis, lupus, sarcoidosis and Crohn's disease eczema.
- **Cancer** (in organs accessible to illumination) such as choriocarcinoma and placenta accrete, bladder and colon.
- **Antibiotics**

Innovative Advantages

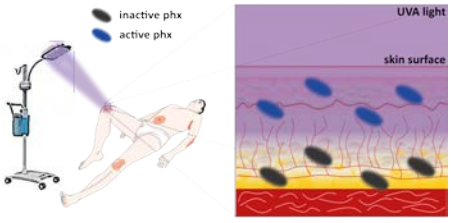
- ✓ Since PHX pharmacologic action **can be reversibly photoregulated**, PHX can become a first-in-class compound in this market segment.
- ✓ PHX **can address many limitations of classical PDT** (1) PDT is not directed to a specific pharmacological target. (2) It requires oxygen as a precursor, which is depleted in hyperproliferative tissues. (3) And irreversibly photogenerated toxic species diffuse to other tissues, causing adverse effects including pain.
- ✓ PHX **can be activated locally** using clinically-approved PDT lamps, and would **self-inactivate upon diffusing** away from the illuminated site, decreasing the occurrence of side-effects.

IBEC
Institute for Bioengineering of Catalonia

EXCELENCIA SEVERO OCHOA

Potential first-in class in photoactivated chemotherapy

Novel nanoscale light-switchable antiproliferative agent



Scientific Project Leader

Dr. Pau Gorostiza
(http://www.ibecbarcelona.eu/nanoprobes)

Stage of development

Successfully done with lead compound:

- ✓ Light-dependent antiproliferative efficacy
- ✓ Safety pharmacology in 55 targets
- ✓ Genotoxicity
- ✓ Cytochrome P450 inhibition
- ✓ *In silico* prediction of *in vivo* toxicity

PoC *in vivo* and further studies ongoing:

- ✓ Pharmacokinetics in mice
- ✓ Cytotoxic efficacy in several cancer cell lines
- ✓ Anti-inflammatory activity in perhipheral blood mononuclear cells (PBMC)
- ✓ Efficacy in imiquimod-induced psoriasis in mice

Intellectual Property Status

PCT/EP2018/086233, December 2018.

Business opportunity

Patent available for licensing with technical cooperation.

Keywords

Psoriasis, chronic inflammatory disorders, cancer, photodynamic therapy, dermatology, antibiotic, chemotherapy, phototherapy.

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