PHX: light-regulated lead compound for the treatment of psoriasis

The Challenge

Severe hyperproliferative diseases of the skin and other tissues (where cells grow without control) 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 has limited their advantages.

The Market

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).

The Asset

We have developed PHX, a light-regulated, target-specific antiproliferative compound (patent pending, including a wide range of analogs). 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. We have assessed the light-dependent antiproliferative efficacy of PHX. Our results in vitro show inhibition of enzymatic activity and arrest of cell growth under illumination at nanomolar PHX concentration, while no antiproliferative effects are observed in the absence of light for a wide range of concentrations (figure a). In zebrafish larvae, the inactive PHX form behaves as the control, whereas light-activated PHX shows effects equivalent to a reference antiproliferative (MTX, figure b). We are currently performing animal assays with PHX.

Product opportunity

Since PHX pharmacologic action can be reversibly photoregulated, PHX can become a first-in-class compound in this market segment. Our approach can potentially address many limitations of classical PDT, which is based on the chemical cytotoxicity of photogenerated species: (1) PDT is not directed to a specific pharmacological target, (2) it requires oxygen as a precursor, which is depleted in hyperproliferative tissues, and (3) 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 diffusion away from the illuminated site. Importantly, by taking the inactivated PHX and only activating it in the skin, we envisage that the treatment will be accompanied with low side-effects.

Scientific Project Leader

Dr. Pau Gorostiza
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Stage of Development

Currently PoC *in vivo* with lead compound.

Intellectual Property Status

EP17382894.8, December 2017.

Exploitation Plan

Licensing and/or co-development.

Contact

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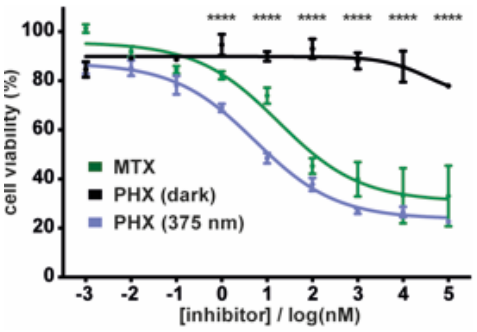

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