Title:

Allergy to the sun: Multidisciplinary investigation on the pathogenesis, treatment and prevention of Polymorphic Light Eruption across Europe (SUNALL)

Objectives:

Polymorphic Light Eruption (PLE) is the commonest sun allergy and affects an estimated 15-20% of the population of Northern Europe. We have gathered a consortium of 6 partners and 2 subcontractors from the United Kingdom, the Netherlands, Germany, Finland, Greece and France who have special expertise in clinical photobiology and experimental photoimmunology, to study the aetiology and pathogenesis of this condition.

The primary objectives of the SUNALL programme of work are to:
- Formulate defined patient diagnostic criteria and standardise methods of assessing and recording severity of sun allergies in different (6) European member states.
- Establish an internet site for patient, health profession and industrial education that will be updated in line with project findings.
- Scientific publications on the development/validation of an empirical model of the pathogenesis of PLE based on disturbances in immunosuppressive responses normally evoked by ultraviolet (UV) exposure; experimental validation in a suitable transgenic mouse model.
- Report/meeting on improved, pan-European diagnostic criteria for PLE (subclasses) and correspondingly better targeted therapies; these diagnostic criteria will be communicated across Europe for critical evaluation by the dermatological experts, and disseminated through professional dermatological organisations, primary care organisations, university education and interested European industrial representatives.
- Final report to EC, with special attention to the necessity of a ‘Health Policy on Sun Allergies’ and ‘Scientific Principles for the Prevention of Sun Allergies’ (strict sun avoidance is likely to worsen the condition).

Scientific approach:

The SUNALL project is split into 5 work packages (WP):

WP1 - We will develop consistent clinical criteria, tools for diagnosis/severity assessment and well-targeted therapies for PLE. This is to be achieved in close linkage with the other workpackages by provision of skin and blood samples for laboratory analyses. These studies will support the model systems for PLE that will be developed in workpackages 4 and 5. The results from the other workpackages will be fed back to the clinical input for the final analysis to establish how the laboratory assays may help to characterise PLE, and so refine diagnosis and provide a basis for targeted therapies. The SUNALL website will be designed and launched.

WP2 - We aim to characterise the in situ deviant reactions in the skin of PLE patients to UV exposure by laboratory analyses (mainly immunohistochemical) of skin biopsies, which are obtained in close linkage with the clinical tests carried out under workpackage 1. Based on the finding that Langerhans cells (LC) remain in the skin of UV overexposed PLE patients, we want to identify the essential deficiency that is either responsible for the relative low threshold for UV-induced erythema or responsible for an inadequate reaction of LC to UV overexposure. To this end, the main focus will be on detection of cytokines known to be relevant to the UV-induced inflammation and immunosuppression, and on the phenotyping of the LC and other immunologically relevant cells.

WP3 - We will establish whether PLE patients are generally hypersensitive to cutaneous allergens and whether their reactivity is inadequately suppressed by UV irradiation, which may allow illicit
immune reactivity against UV-induced neo-antigens. We will therefore (a) compare the ability of PLE patients and healthy volunteers to mount immunological reactivity to an experimental contact allergen; (b) compare the ability to downregulate that immune reactivity when the sensitisation site is exposed to an erythematogenic dose of UV radiation before sensitisation; (c) compare the relationship between UV erythemal reactivity and the aforementioned immunological parameters; (d) compare the effect of a preceding series of suberythemic UV exposures, i.e. hardening treatment, on the erythemal and immunological parameters; (e) compare the response of LC to migratory stimuli other than UV radiation.

WP4- We will establish whether samples of uninvolved skin and/or blood cells from PLE patients show aberrant immune reactions in well-controlled in vitro assays, or whether immune reactions against UV irradiated skin (fractions) can be evoked in in vitro assays (as a model of PLE). Considering the aberrant reaction of LC in PLE patients to UV overexposure, we will focus on the function of these LC, on the potentially responding T cells in the blood or residing in the skin, and on circulating mononuclear cells which can be manipulated to produce dendritic cells with the LC phenotype.

WP5- We aim to provide animal-experimental proof that aberrant activation and/or migration of LC upon UV irradiation of the skin can simulate PLE, and thus explain the condition. The threshold for UV-induced release of inflammatory mediators appears relatively low in PLE patients in comparison to the threshold for the disappearance of LC from the skin. Thus, PLE might be a disease in which acute UV exposure tends to activate, rather than inactivate cutaneous LC, and leave these LC present in the skin. To test this hypothesis we will compare mice that have defective LC activation (and defective migration) and those that have constitutively activated LC.

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