An Inflammatory-Driven Ex Vivo Human Skin Model to Mimic Atopic Dermatitis–Like Barrier Dysfunction

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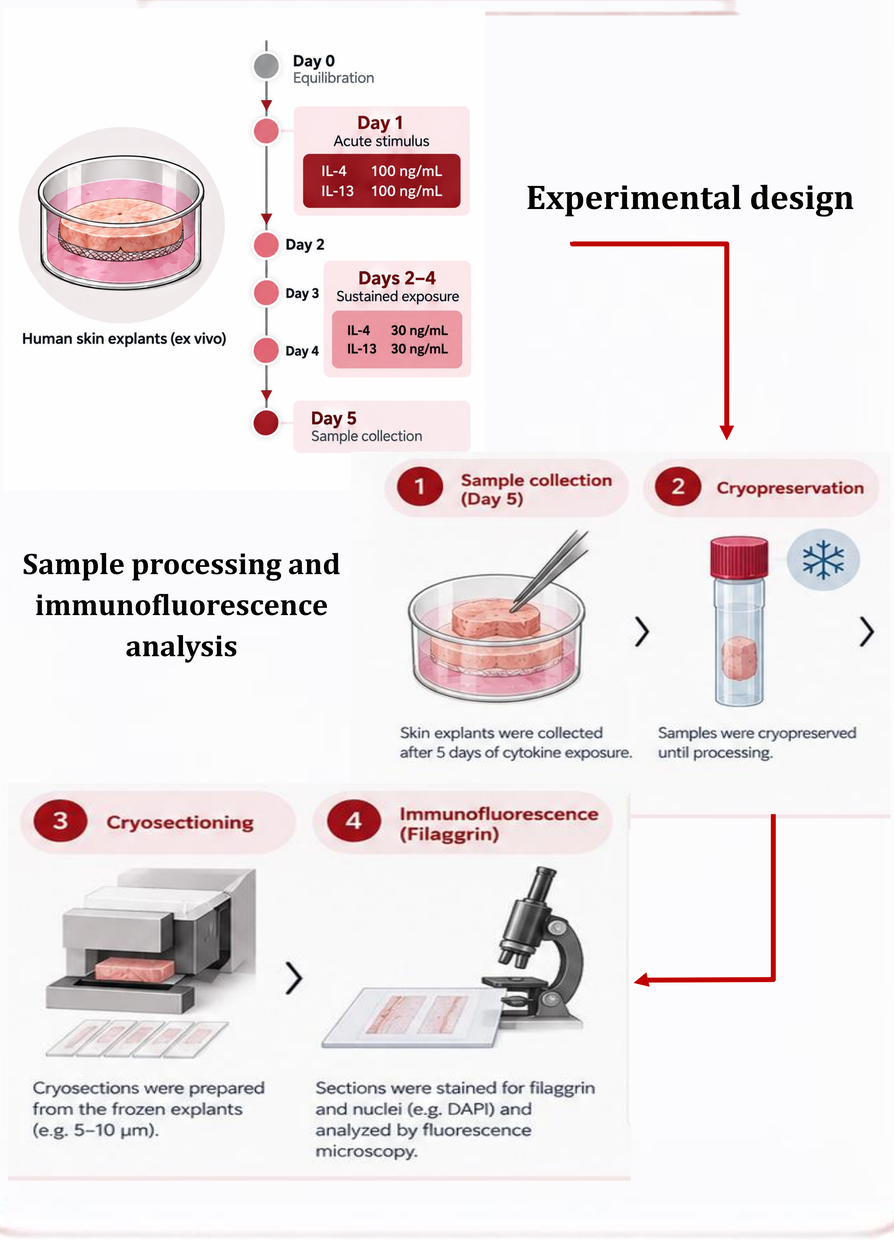
INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease involving epidermal barrier dysfunction, immune dysregulation, and altered host–microbiome interactions. Central to its pathogenesis is a Th2-skewed immune response, characterized by elevated levels of interleukin-4 (IL-4) and interleukin-13 (IL-13), which directly impair keratinocyte differentiation and downregulate epidermal key structural proteins such as filaggrin. The resulting barrier disruption promotes increased transepidermal water loss, enhanced penetration of allergens and irritants, and heightened susceptibility to microbial colonization, perpetuating a vicious cycle of inflammation and barrier impairment.

OBJECTIVES

To establish a human ex vivo skin model that reproduces key molecular and functional features of AD-like inflammation, particularly epidermal barrier disruption.

MATERIALS AND METHODS



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RESULTS

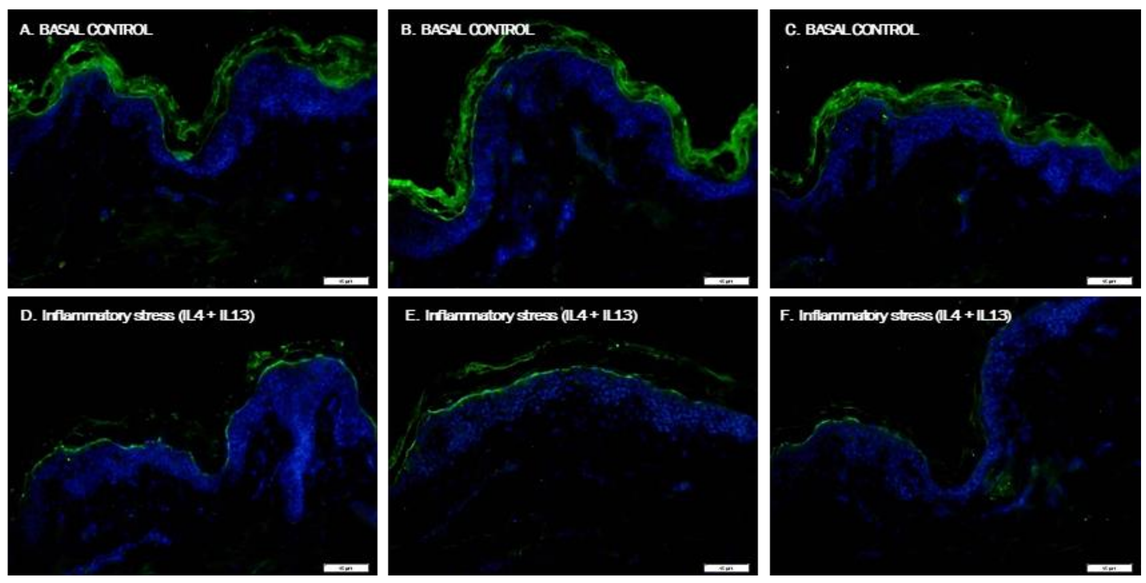


Figure 1: Micrographic evaluation of filaggrin labeling in human ex-vivo skin fragments exposed to the inflammatory stress. A-C: Untreated skin fragments (Basal Control). D-F: Skin fragments exposed to the inflammatory stress protocol (IL-4 + IL-13). The filaggrin are marked in green and the blue marking represents the nucleus of the cell (DNA; DAPI). The reference bar corresponds to 50µm.

51.56% ↓

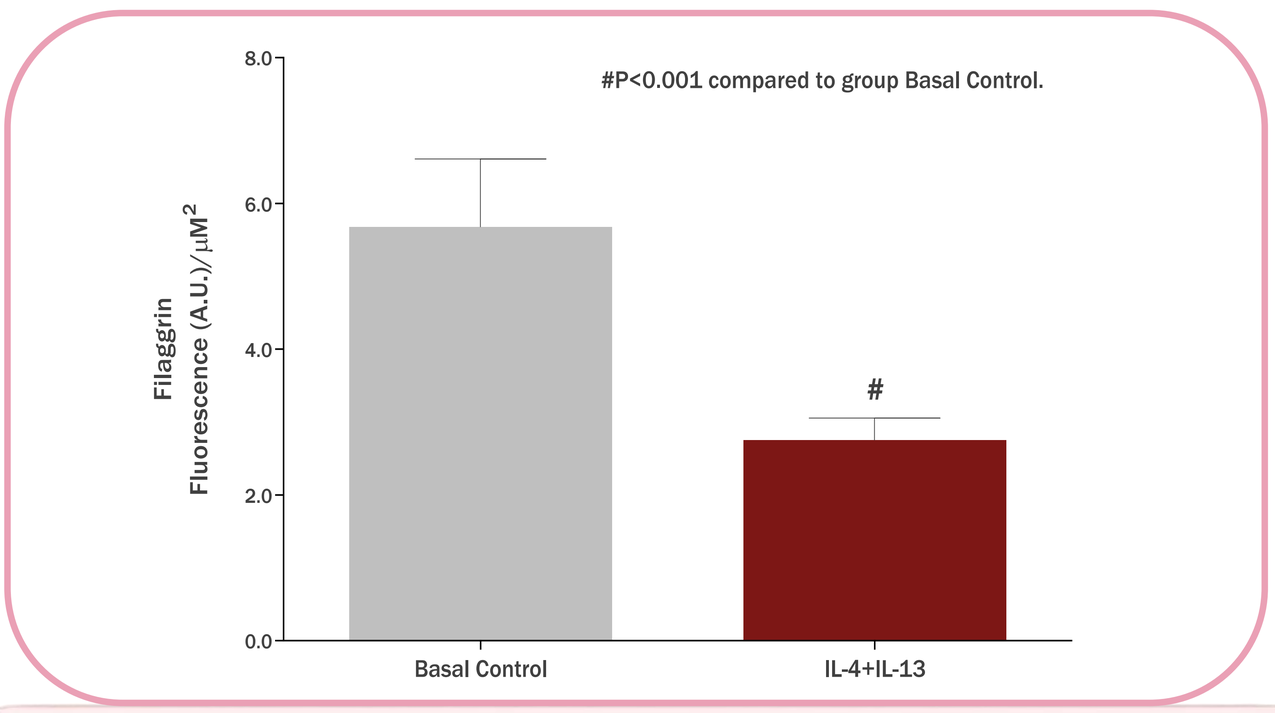


Figure 2: Effect of the inflammatory protocol on the production of filaggrin in human ex-vivo skin fragments exposed to IL-4 + IL-13. Data represent the mean ± standard deviation of 06 replicates (Student's T-test).

DISCUSSION

Cytokine exposure resulted in a marked and statistically significant reduction in filaggrin expression (−51.56% vs. basal control, $P < 0.001$), confirming the effective induction of a barrier-disrupted phenotype consistent with AD pathophysiology. The magnitude of this reduction highlights the critical role of IL-4 and IL-13 in driving structural impairment of the epidermis and supports the translational relevance of the model.

Taken together, these findings demonstrate that this human ex vivo skin model reliably reproduces key immunopathological features of atopic dermatitis, particularly those associated with Th2-mediated barrier dysfunction. This platform represents a robust, reproducible, and ethically relevant tool for dermatological research, with strong potential for investigating disease mechanisms and supporting the preclinical evaluation of therapeutic and dermocosmetic interventions targeting barrier restoration in patients with AD and sensitive skin conditions.

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