PUBLISHED ABSTRACT

RNAseq Profiling Highlights Immune and Barrier Differences among Ichthyoses

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Transcriptional analyses of a small sample of patients with rare forms of ichthyosis have suggested a shared Th17-skewed profile. To elucidate pathogenic differences among ichthyoses, we performed RNAseq on skin of a large cohort (n = 56) ichthyosis patients (7 Netherton syndrome/NS, 16 lamellar ichthyosis/LI, 18 congenital ichthyosiform erythroderma/CIE, 13 epidermolytic ichthyosis/EI, and 2 ichthyosis with confetti/IWC) vs. 40 matched controls. Using FCH > 2 FDR < 0.05 criteria, we found increased markers of T-cell activation/migration (ICOS, CCR7) and Th17/Th22 (IL17A/F, IL36G, S100s, PI3) across ichthyoses. IL-17/TNF-α-induced markers (e.g., VNN3, KYNU, PI3, DEFB4) were highest in the more erythrodermic forms (NS, CIE, IWC) and lowest in EI. Th22/IL22 expression was more elevated in NS and CIE than other forms and CIE specifically showed very high increases in Th1/IFN-related responses (IL12B, IL1B, CXCL9/10). Th2 cytokines IL4 and IL13 markers were reduced in ichthyosis, but IL4R was particularly high in NS and CCL18 in NS and CIE. Terminal differentiation genes (e.g. FLG) were generally increased in ichthyoses, except LOR that was decreased in NS, CIE, and IWC. Claudin gene expression was reduced universally, but reduction of lipid-related gene expression (ie, FADS1, ELOVL3, FAR2, FA2H) was greatest for LI and significant for NS and CIE, but not EI or IWC. Enrichment analyses highlighted cell cycle targets in all ichthyosis and pathways upregulated by IL6/STAT3 in CIE and EI. Our broad skin profiling of ichthyoses highlights immune and barrier-specific landscapes that may require alternative therapeutic modulation.

Author Contribution

Guttman-Yassky author contributed equally to this manuscript.

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