PNAS RESEARCH ARTICLE | IMMUNOLOGY AND INFLAMMATION

CD2 expressing innate lymphoid and T cells are critical effectors of immunopathogenesis in hidradenitis suppurativa

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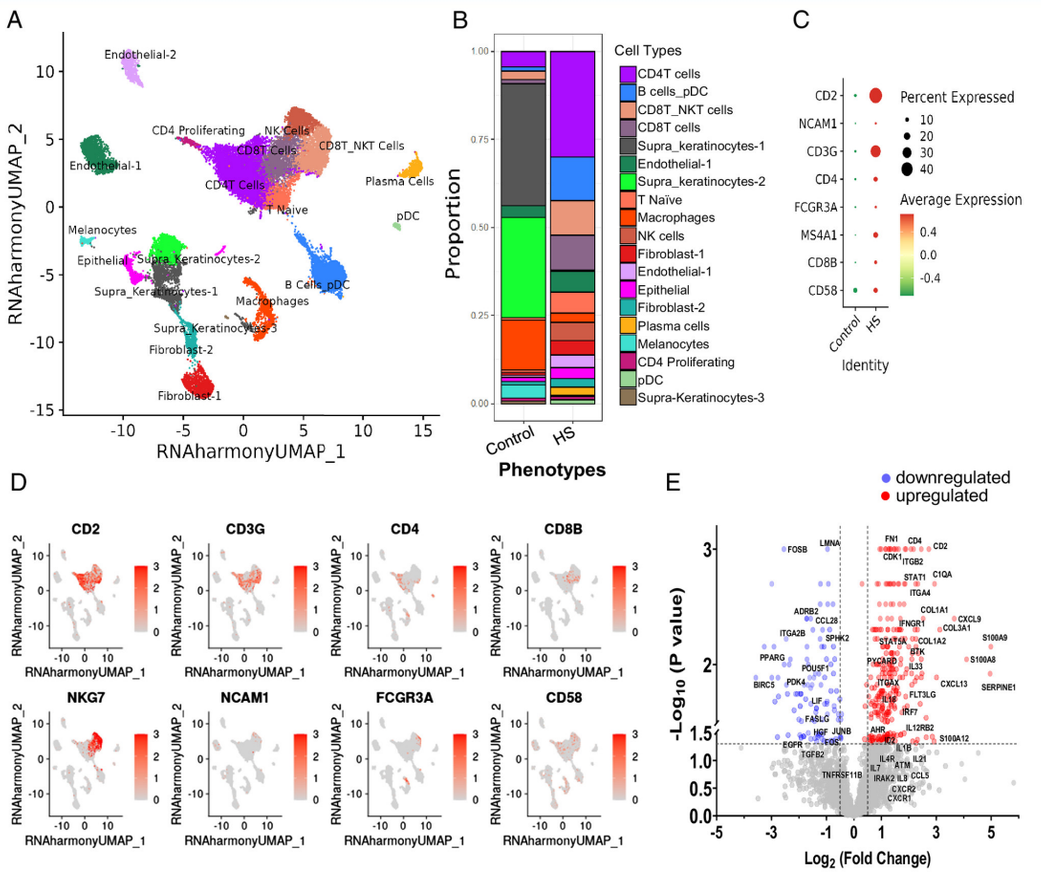
Significance

Hidradenitis suppurativa (HS) is a progressive, debilitating inflammatory disease with poorly defined etiology and incompletely characterized cell populations driving its pathogenesis. Our study identifies that CD2, an activation and adhesion receptor, is expressed at elevated levels on T cells and on innate lymphoid cells [natural killer (NK)/innate lymphoid cell 1 (ILC1), natural killer T (NKT), mucosal-associated invariant T (MAIT)]. We further report that disruption of the cognate interaction between CD2 and its ligand, CD58, is a therapeutic target for the treatment of HS. Importantly, our data suggest that distinct subpopulations of NKT and NK cells are the major drivers of HS disease pathogenesis.



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Integrative systems biology framework discovers common gene regulatory signatures in mechanistically distinct inflammatory skin diseases

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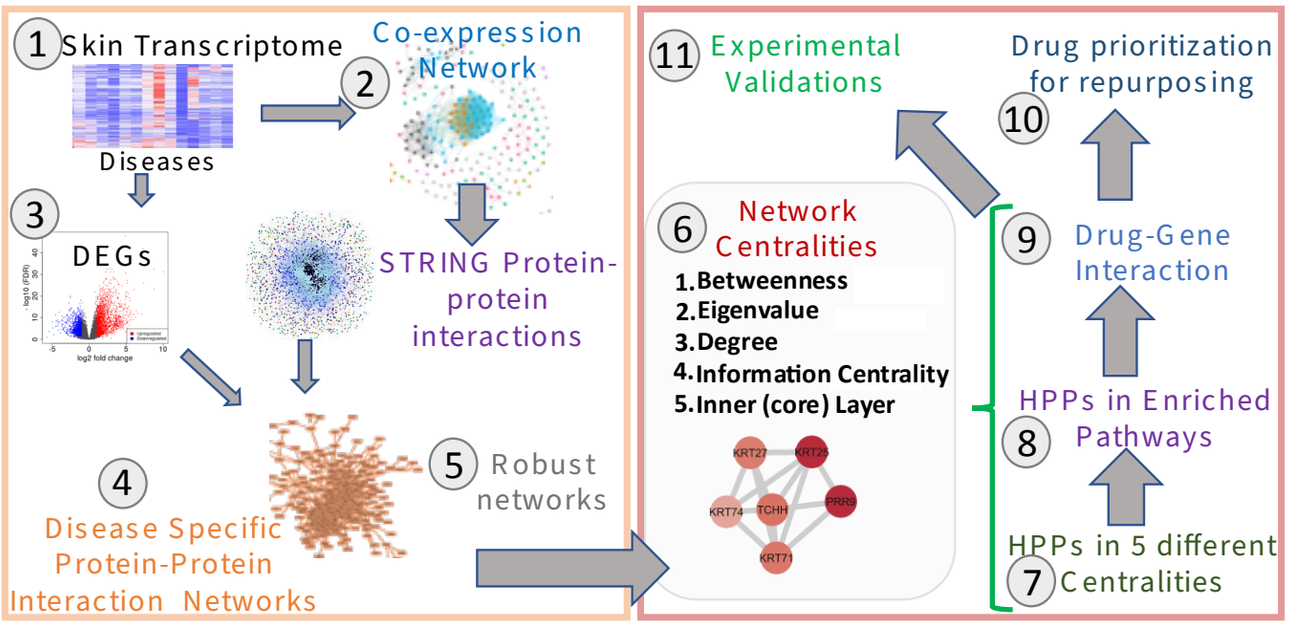
More than 20% of the population across the world is affected by non-communicable inflammatory skin diseases including psoriasis, atopic dermatitis, hidradenitis suppurativa, rosacea, etc. Many of these chronic diseases are painful and debilitating with limited effective therapeutic interventions. This study aims to identify common regulatory pathways and master regulators that regulate the molecular pathogenesis of inflammatory skin diseases. We designed an integrative systems biology framework to identify the significant regulators across several diseases. Network analytics unraveled 55 high-value proteins as significant regulators in molecular pathogenesis which can serve as putative drug targets for more effective treatments. We identified IKZF1 as a shared master regulator in hidradenitis suppurativa, atopic dermatitis, and rosacea with known disease-derived molecules for developing efficacious combinatorial treatments for these diseases. The proposed framework is very modular and indicates a significant path of molecular mechanism-based drug development from complex transcriptomics data and other multi-omics data.



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A rice protein interaction network reveals high centrality nodes and candidate pathogen effector targets

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ABSTRACT

Network science identifies key players in diverse biological systems including host-pathogen interactions. We demonstrated a scale-free network property for a comprehensive rice protein–protein interactome (RicePPInets) that exhibits nodes with increased centrality indices. While weighted *k*-shell decomposition was shown efficacious to predict pathogen effector targets in Arabidopsis, we improved its computational code for a broader implementation on large-scale networks including RicePPInets. We determined that nodes residing within the internal layers of RicePPInets are poised to be the most influential, central, and effective information spreaders. To identify central players and modules through network topology analyses, we integrated RicePPInets and co-expression networks representing susceptible and resistant responses to strains of the bacterial pathogens *Xanthomonas oryzae* pv. *oryzae* and *X. oryzae* pv. *oryzicola* (*Xoc*) and generated a RIce-*Xanthomonas* INteractome (RIXIN). This revealed that previously identified candidate targets of pathogen transcription activator-like (TAL) effectors are enriched in nodes with enhanced connectivity, bottlenecks, and information spreaders that are located in the inner layers of the network, and these nodes are involved in several important biological processes. Overall, our integrative multi-omics network-based platform provides a potentially useful approach to prioritizing candidate pathogen effector targets for functional validation, suggesting that this computational framework can be broadly translatable to other complex pathosystems.