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Case Study: Mapping Disease Pathways in Epidermolysis Bullosa Using Mavatar Discovery

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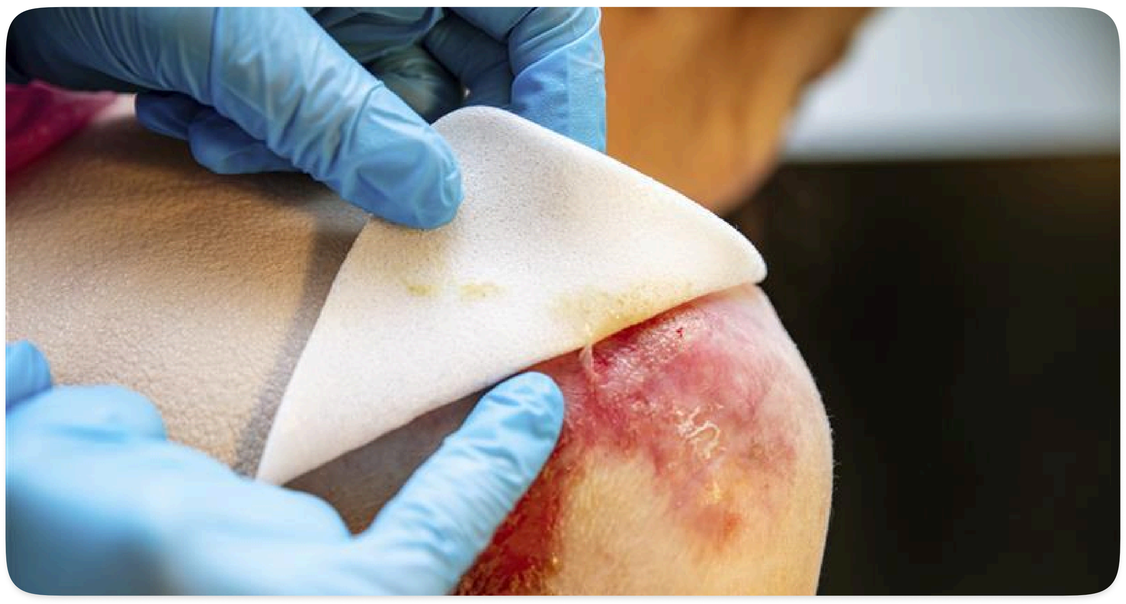
Background

Epidermolysis Bullosa (EB) is a rare connective tissue disorder manifesting with extreme skin fragility and blister formation in response to minor friction or physical trauma. It has several major subtypes defined by their skin separation level, and the main causes for the disease are mutations in genes encoding proteins essential for skin integrity, specifically those involved in dermal-epidermal adhesion (reviewed by Has et al). The disease brings with it an extreme amount of suffering, both physical and mental due to physical pain and a lack of treatment options. Currently, disease treatment focuses on managing symptoms such as wound care and preventing infections. New therapeutics focus on gene therapy and protein replacement, where finding new protein targets holds an important place.

Using our Mavatar Discovery Platform, which enables disease modeling at the systems level through analysis of thousands of transcriptomics datasets, we aimed to identify context-specific gene networks for EB.



Challenge

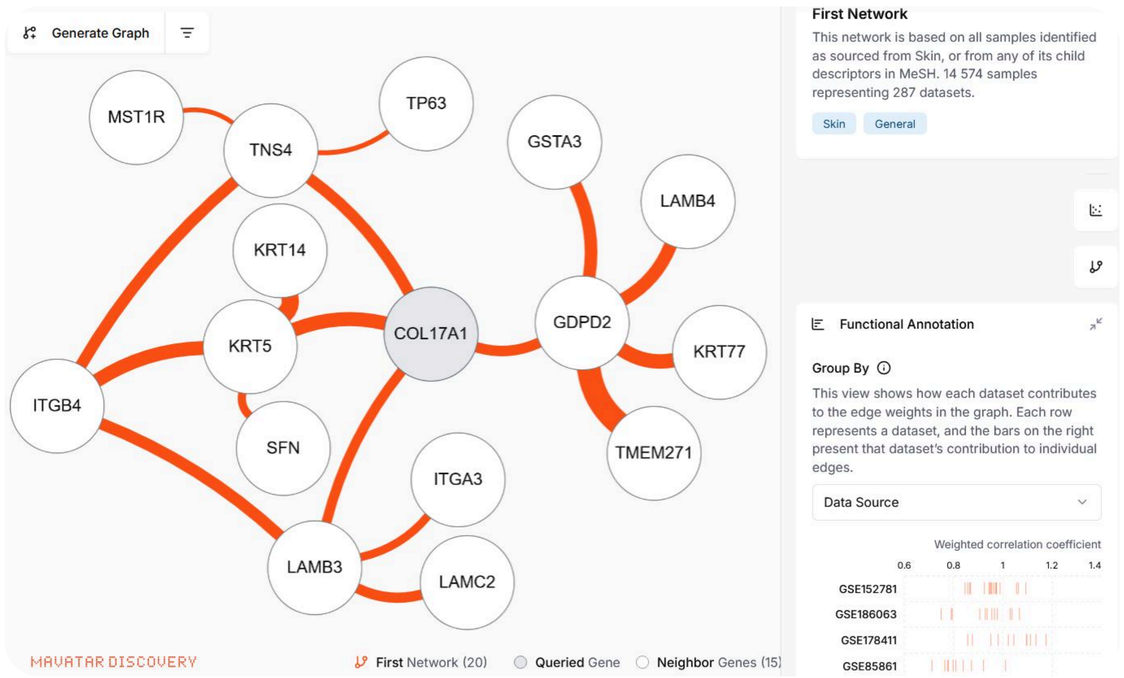
Even though the genetic basis of EB is partially known, it remains difficult to reconstruct a complete molecular disease pathway. Conventional tools lack the integration of tissue-specific context and fail to reveal functional connections among known and emerging genes, limiting the identification of therapeutic targets or modifier pathways.

Solution

We used our comprehensive skin disease data resource, including conditions such as psoriasis, atopic dermatitis, and blistering disorders, to create gene networks for different EB targets. Investigation of EB simplex focusing on KRT5 and KRT14 mutations created a network including COL17A1, ITGB4, LAMB3, and LAMC2 in close proximity—genes associated with junctional EB mutations.

Results

The analysis revealed two core disrupted systems in EB: laminin/integrin complexes and keratin structures. Notably, 6 of the 14 other known EB genes were significantly enriched in the neighborhood of COL17A1 -- a >700x enrichment vs. random ($p < 0.00001$). Researchers also found new candidate genes involved in cell adhesion and wound healing, co-expressed in the same skin layer, and implicated in EB comorbidities such as skin cancer.



Conclusion

Our systems-level approach successfully identified interconnected gene networks across EB subtypes, revealing shared molecular pathways that could serve as therapeutic targets, including the cornification and estrogen pathways. These findings demonstrate the potential of computational network analysis in therapeutic discovery for complex and rare diseases.

About Mavatar Discovery

Mavatar Discovery is a self-service, cloud-based research platform for pharma, biotech, and academic teams. Unlike traditional tools, it uses fully data-driven, real-time analysis to model disease mechanisms and reveal new therapeutic opportunities.

- From raw RNA-seq to translational insight — no coding, no delays
- Accelerated hypothesis generation — turn complex data into testable ideas
- Uncover biomarkers and disease mechanisms faster
- Thousands of transcriptomes in one integrated, searchable platform
- A smarter starting point for next-generation therapies

Want access to Mavatar Discovery?

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Disclaimer:
This case study is an example, created for illustrative purposes to demonstrate the capabilities of the Mavatar Discovery platform.

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