Institution	Project Name	Project Description	Patient Population	Technique	Principal Investigator(s)	Amount Funded (EBRP)
Stanford University	Randomized Controlled Trial of a Neurokinin-1 Receptor Antagonist for the Treatment of Pruritus in Patients with Epidermolysis Bullosa	Itch, or pruritus, is the most common complaint reported by epidermolysis bullosa (EB) patients of all subtypes, and there is no effective treatment. Itch often triggers scratching that creates new wounds and increases disease severity. Current management of EB itch is unsatisfactory. Substance P is a major mediator of pruritus and binds to the neurokinin-1 (NK1) receptor. We recently evaluated the effects of serlopitant, an oral inhibitor of the NK1 receptor, in an exploratory randomized trial for the treatment of EB itch in 14 patients. We observed a small magnitude reduction in NRS itch severity in favor of serlopitant relative to placebo (0.08 point/week comparative reductio) over 8 weeks, although this difference did not meet the statistical significance (p=0.11). Given these promising results, we intend to pursue a better powered 40 patient randomized controlled trial for patients 13 years and older to better assess the efficacy of serlopitant for EB itch.	All	Wound Healing Topic	Albert Chiou MD, Jean Y Tang MD PhD	$37,500.00
Stanford University/ GeneDX	AWS x Stanford x GeneDX 50 Patient Genomic Sequencing Pilot	EB Research Partnership (EBRP), Stanford Medicine, and AWS are building a first of its kind collaborative digital platform to unite Investigators (Doctors and Researchers) with patients and families. The platform leverages the power of clinical information like phenotype and genotype data, EHRs, and clinical trials and combines it with social connectivity and direct patient participation to accelerate treatments and cures for EB. The platform also utilizes genomic reporting from GeneDX.	All	Data	Jean Y Tang MD PhD	$40,000.00
AWS	Direct to Patient Platform	EB Research Partnership (EBRP), Stanford Medicine, and AWS are building a first of its kind collaborative digital platform to unite Investigators (Doctors and Researchers) with patients and families. The platform leverages the power of clinical information like phenotype and genotype data, EHRs, and clinical trials and combines it with social connectivity and direct patient participation to accelerate treatments and cures for EB. The platform also utilizes genomic reporting from GeneDX.	All	Data	Jean Y Tang MD PhD	$190,100.00
University of Minnesota	Autologous Revertant Mosaic Fibroblasts for Wound Healing in Dystrophic Epidermolysis Bullosa	DEB patients lack adequate and normal type VII collagen (C7) to hold the layers of skin together. With few effective therapies and no cure available, therapies that reduce pain and improve quality of life are critical. Naturally occurring genetic events can correct the DEB-causing mutation in fibroblasts, restoring functional protein production in that location and creating revertant mosaic patches of unaffected skin. We have shown near-normal C7 production in revertant mosaic fibroblasts and are currently refining new methods to identify and isolate these cells from punch biopsies from DEB patients with revertant mosaic skin. The revertant mosaic fibroblasts can then be cultured in clinically impactful numbers and used intradermally, or intravenously to home to less accessible areas that could benefit from C7. We will use revertant mosaic fibroblasts intradermally to assist in wound report and tissue regeneration in a two-year clinical trial of 10 patients to evaluate effectiveness and safety.	RDEB	Immunotherapy Cancer Research	Jakob Tolar, MD	$327,837.00
University of Southern California	Repurposing Anti-malarial Artemisinin to Inhibit RDEB Fibrosis and Scarring	Patients with recessive dystrophic epidermolysis bullosa (RDEB) develop multiple skin wounds that heal with extensive scarring causing subsequent contractures and mitten deformities. RDEB patients display increased pro-fibrotic TGF-β signaling and a distinct pro-fibrotic/pro-inflammatory gene expression profile. No specific treatment is available for RDEB fibrosis. Artemisinin is a safe, FDA-approved, antimalarial medication with anti-inflammatory and anti-fibrotic properties. In this proposal, we will determine if artemisinin reverses the hyper-contractibility of cultured RDEB fibroblasts and reduces their levels of pro-fibrogenic TGF-β and fibrosis markers. We will also administer artemisinin to RDEB-like mice and see if it inhibits mitten deformities and digit loss while also inhibiting markers of fibrosis and pro-fibrogenic TGF-β in the skin. If successful, this study will provide the basis for clinical trials in RDEB patients and evaluating the potential of re-purposed artemisinin for reducing fibrosis, scarring and contractures and improving the quality of life of RDEB patients.	Dystrophic EB (DEB)	Drug Repurposing	Mei Chen, David Woodley	$183,750.00
Department of Dermatology and Institute for Augemnted Intelligence in Medicine, The Feinberg School of Medicine Northwestern University	Augmented Intelligence in EB: Using deep learning for early detection of squamous cell carcinoma in EB	Squamous cell carcinoma (SCC) metastasizes quickly and is the most common cause of death in young adults with recessive dystrophic EB (RDEB). Even for experts, distinguishing SCCs from "normal" RDEB skin and finding the optimal biopsy site is difficult. Challenges with routine full-body examination and patient fears of biopsy further delay SCC diagnosis, reducing treatment success and survival. Given the high potential of augmented intelligence in recognizing skin cancer, we are developing a deep learning network to provide a low-threshold tool for early detection of RDEB-SCCs. During ongoing year 1, we are developing the deep learning technology, based on thousands of photos of RDEB skin and SCCs that we are collecting through an international network. In year 2, the tool will be validated and transferred into a web application. Our long-term goal is a tool for interpretation of RDEB skin photography to assist in fighting SCCs as early as possible.	Dystrophic EB (DEB)	Cancer Research Data	Amy Paller, Antonia Reimer-Taschenbrecker, Abel Kho	$464,072.00
Thomas Jefferson University	Repurposing daclatasvir for RDEB therapy	Recessive Dystrophic Epidermolysis Bullosa (RDEB) is a devastating skin blistering disease for which currently there is no cure. The severity of RDEB correlates directly with the degree of fibrotic reaction in the skin; therefore approaches to inhibit fibrosis will likely improve patient quality of life. Our preliminary data shows that the anti-viral drug daclatasvir extends the lifespan of the RDEB hypomorphic mouse (Fig.1) and this funding application seeks to understand the relationship between daclatasvir, RDEB survival and an emerging secretory defect resulting from loss of full-length type VII collagen, the protein which is defective in patients with RDEB. This application will test the evolving central hypotheses that 1) targeting a secretory defect in RDEB will ameliorate fibrosis and improve survival in patients with RDEB 2) the FDA-approved compound daclatasvir will show measurable improvement in RDEB survival in vivo using preclinical mouse models.	Dystrophic EB (DEB)	Drug Repurposing	Andrew South	$97,727.00
Thomas Jefferson University	Rigosertib for recessive dystrophic epidermolysis bullosa-associated squamous cell carcinoma	Squamous cell carcinoma (SCC) of the skin is the biggest cause of death in patients with recessive dystrophic epidermolysis bullosa (RDEB). Although emerging data are identifying why patients suffer this fatal complication, therapies which target RDEB SCC are urgently required. We previously identified a lead compound, ON-01910 (rigosertib) that exhibited significant specificity for RDEB cancer: rigosertib induced apoptosis in 10/10 RDEB SCC keratinocyte populations without affecting normal RDEB skin cells in culture. Based on this data we initiated a "first in EB" clinical trial of rigosertib to assess tolerability and tumor targeting in patients with late stage, metastatic and/ or unresectable SCC. The first patient to be treated with rigosertib in Europe has shown a complete response with all three target lesions being eliminated after six months. This application is to fund treatment of three patients in the US with intravenous rigosertib.	Dystrophic EB (DEB) Junctional EB (JEB)	Cancer Research	Andrew South, Neda Nikbakht	$332,620.00

Stanford University	Validation of an Investigator's Global Assessment Scale for Assessing Disease Severity in Epidermolysis Bullosa Simplex Clinical Trials	Clinical measures of disease severity in epidermolysis bullosa (EB) are critical for evaluating novel therapies, and lack of validated measures can prove a substantial regulatory barrier for new treatments. There are no validated scales specifically designed for epidermolysis bullosa simplex (EBS)-related wounds. Given the focus of recent trials on topical therapies for EBS, we propose here a rigorous instrument validation study for the previously reported Investigator's Global Assessment (IGA) for disease severity in EBS. Given FDA guidance to minimize travel for EB trials, we will evaluate the instrument's validity and reliability when applied to digital photographs of target lesion areas obtained from virtual evaluations conducted with 10 pediatric and 10 adult EBS participants. Up to 50% of the cohort will participate in a one day clinic scoring exercise to evaluate comparative performance in person vs. virtually. We anticipate validation of the IGA will improve the feasibility of future EBS trials.	EB Simplex (EBS)	Data	Albert Chiou, Jean Tang, Eleni Linos	$106,582.00
Future Industries Institute	Development of a systemic antibody therapy for the treatment of epidermolysis bullosa.	Notwithstanding the horrific impact of lifelong blistered skin, EB patients also have to deal with the major challenge of living with chronic ulceration of their internal mucosal surfaces. These oral, oesophageal and gastrointestinal ulcerations lead to malnutrition, malabsorption, constipation and a failure to thrive which dramatically reduces the lifespan of people with EB. Our research has identified Flightless I (Flii) as a target protein that contributes to impaired healing of both external skin wounds and internal gastric ulcers. We have developed a monoclonal Flii neutralising antibody that when administered systemically to mice with either skin wounds or IBD improves healing and reduces the severity of intestinal ulcerations. To progress our antibody therapy into human clinical trials we need to select, characterise and humanise our lead antibody candidate. This will facilitate the development of a systemic therapy that could lead to a simple and effective new treatment for EB patients.	EB Simplex (EBS) Dystrophic EB (DEB) Junctional EB (JEB) Kindler Syndrome		Allison Cowin, Zlatko Kopecki	$252,802.00
APTEEUS, University of Freiburg	TEE002 repositionning in epidermolysis bullosa	RDEB is characterized by skin fragility leading to blisters and lesions. Chronic inflammation, responsible for overactivation of skin fibroblasts and differentiation into myofibroblasts, participates in skin fibrosis, atrophic scars and finally squamous cell carcinoma. TEE002 is of particular interest in addressing several pathophysiological mechanisms of RDEB. It is a safe molecule marketed for its anti-inflammatory properties. In silico and in vitro analysis showed the potential of the drug to limit fibrosis through an inhibition of TGFβ/Activin pathway. Considering its excellent safety profile both orally and topically, and after demonstrating its efficacy in vitro, we intend to prove its efficacy in vivo on the collagen VII hypomorphic mouse developed by the University of Freiburg. This model will enable the demonstration of the expected benefit of TEE002 on inflammation, fibrosis and scar formation, and lead to an in vivo proof-of-concept before engaging efforts in a pharmaceutical and clinical development.	Dystrophic EB (DEB)	Drug Repurposing	Terence Berghyn, Alexander Nystrom, Thibaut Vausselin	$259,000.00
Centre for Human Genetics	Development of a Registry for Epidermolysis Bullosa in India	India is a large country with respect to land area and population. The population is very diverse in ethnicity with a high degree of consanguinity. Our data on clinical, immunofluorescence and genetic studies show a lot of heterogeneity. India lacks a structured registry for EB patients. Establishing a registry including clinical and genotype information would help us in building a database for future clinical trials when it becomes feasible. At Centre for Human Genetics, we have established structured multi-disciplinary clinics for EB. During the conference on EB last year, we have established a network of clinicians to interested in caring for EB patients. Thus, we propose to use technology-based strategy to initiate a registry for EB in the state of Karnataka.	All	Data	Ravi Hiremagalore MD, Gurudatta Baraka PhD, Arun Inamadar MD, Sacchidanand MD	
Phoenicis		Based on an insight that skin diseases are inherently inflammatory diseases, Phoenicis decided to focus on first-in-class treatments for rare, genetic, and inflammatory diseases with multiple "shots on goal" for orphan, breakthrough, and pediatric designations. This holding company has partnered with other disease organizations to bring other assets into the holding company. The holding company is looking to raise capital and to leverage its assets more broadly than just EB.				$1,000,000.00
Stanford University	Optimizing induced Skin Composite Delivery Through Electrospray-on-Skin Technology	While our autologous, genetically-corrected induced pluripotent dystrophic EB cell therapy (DEBCT) demonstrates both pre-clinical efficacy and safety, delivery of the induced skin composite (iSC) consisting of epidermis, dermis and melanocytes to topologically-challenging body wounds remains problematic. Next generation electrospray-on-skin technologies use inert porous matrix to optimize cellular adherence and tissue polarization. We have partnered with Nanomedic and demonstrated that electrosprayed keratinocytes and fibroblasts spontaneously form skin tissue within the nanofiber matrix in a new model of murine wound healing, motivating our overarching hypothesis that electrosprayed DEBCT followed by SpinCare matrix will facilitate patient wound closure. We will test our hypothesis by elucidating the cellular composition parameters for murine wound healing and validating DEBCT cellular composition for optimal murine wound healing. Successful completion will provide critical optimal DEBCT cellular composition for clinical delivery for the updated Pre-IND package and pave the way for IND enabling studies for Phase I DEBCT trial.	EB Simplex (EBS) Dystrophic EB (DEB) Junctional EB (JEB) Kindler Syndrome	Stem Cell Therapy	Anthony Oro	$288, 478.00
Eliksa Therapeutics	Development of a Novel Ophthalmic Solution to Treat Ocular Manifestations of Recessive Dystrophic Epidermolysis Bullosa	Eliksa Therapeutics is developing a novel ophthalmic solution (ELK-003) to treat the ocular manifestations of Recessive Dystrophic Epidermolysis Bullosa. We are proposing a pilot investigator-sponsored clinical trial to evaluate the safety and efficacy of ELK-003 in Epidermolysis Bullosa (EB). ELK-003 is also being tested in 5 other clinical trials (non-EB related) at the University of Utah with 140+ patients already enrolled and with no adverse events reported. ORA Clinical, an ophthalmic-focused contract research organization (CRO) with experience in approving 56+ ocular drugs, has been engaged by Eliksa to provide regulatory guidance and support for this indication. In addition, Eliksa has entered into a one-year sponsored research agreement with Dr. Andrew South at Thomas Jefferson University to further elucidate the mechanism of action of ELK-003 in the context of EB. For this grant we are seeking funds to advance the development of ELK-003 as a treatment for ocular manifestation of EB.	Dystrophic EB (DEB)	Protein Therapy	Armen Karamanian, John Phillips, Andrew South, Vicki Chen, Francis Palisson, Ignacia Fuentes, Arturo Kantor, and Felipe Mellado	$850,000.00
University of Colorado Anschutz Medical Campus	Adapting the induced pluripotent stem cell-based therapy for recessive dystrophic epidermolysis bullosa to an automated platform to facilitate clinical translation	We are developing a stem cell-based gene correction therapy for Epidermolysis Bullosa (EB) using autologous induced pluripotent stem cells (iPSCs) derived from skin cells harvested from the same EB patient. To date, we have developed all critical steps of this therapy. We produce corrected EB iPSCs using our patented combined gene editing and reprogramming approach. We generate iPSC-derived keratinocytes and fibroblasts via organoids. We will deliver these cells via a "spray-on-skin" system, and we have developed a mouse xenograft model that simulates this type of skin cell delivery for safety studies. Since the production of corrected RDEB iPSCs and skin organoids requires extensive manual manipulations, here we propose to adapt our combined gene editing and reprogramming and the derivation of skin organoids to an automated cell-picking platform. The use of this automated platform will simplify the production of iPSCs and organoids, making our therapy more cost effective and commercially viable.	Dystrophic EB (DEB)	Stem Cell Therapy	Dennis Roop, Ganna Bilousova, and Igor Kogut	$999,724.00

Stanford University	A Randomized Phase 2 Clinical Trial to Evaluate a Temporary Skin Substitute (Spincare™ Matrix) for Wound Healing in RDEB patients	RDEB patients may develop large, painful wounds that do not heal and require frequent extensive full-body dressing changes that take several hours to perform. Each daily dressing change introduces the possibility of retraumatizing the skin and is often tremendously painful. The standard of care is primarily prevention of trauma and supportive care for wound healing using non-adhesive bandages. The Spincare matrix is the first portable device that delivers an electrospun, nanofibrous dressing for wound healing. Previously, it is approved in Europe for the treatment of burn wounds. The aim of this pilot study is to determine the suitability of Spincare™ nanofibrous matrix in RDEB wounds and assess its wound healing properties and safety signals. We anticipate that the results of this study will aid in future research to demonstrate the Spincare™ system as an acceptable and safe device for delivery of gene-corrected cells into RDEB wounds.	Dystrophic EB (DEB)	Stem Cell Therapy	Jean Tang and Dawn Siegel	$744,145.00
Cincinnati Children's Hospital Medical Center	Evaluation of Squamous Cell Carcinoma in Recessive Dystrophic Epidermolysis Bullosa: Clinical, Molecular, and Pathologic Characteristics and Outcomes	Patients with recessive dystrophic epidermolysis bullosa (RDEB) can develop aggressive and often lethal squamous cell carcinomas (SCCs). We aim to create a detailed retrospective database for each of our 17 current RDEB SCC patients, and prospectively track new patients. It will include clinical, histologic, and imaging data as well as and clinical outcomes including response to treatment, recurrence, and chemoprophylaxis. We will also re-evaluate SCC samples histologically and will stain for additional immunohistochemistry markers (e.g., TGFB, IL6, periostin, decorin, etc.). We will perform genomic analysis of these samples. We aim to correlate molecular markers and mutations with clinical characteristics and outcomes. We hope to also determine if these is a role for chemoprophylaxis. Our ultimate goal is to evaluate if any of these markers could be used as targets for either new therapies or re-purposed existing therapies.	Dystrophic EB (DEB)	Drug Repurposing Cancer Research Data	Anne Lucky, Emily Gorell, and Brian Turpin	$351,121.00