be well informed and family/community-centered, and that will strengthen the persistence, support network, and patient empowerment to translate confidence into sustained glycemic control.

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Sphingosine-1-phosphate deficiency drives skin injury after Staphylococcus aureus infection

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OBJECTIVES/GOALS: We aim to determine whether inadequate sphingosine-1-phosphate (S1P) production in hyperglycemia is involved in deranged inflammatory response and host defense during methicillin-resistant Staphylococcus aureus (MRSA) skin infection. METHODS/STUDY POPULATION: Using a Phenome-Wide Association Study (PheWAS), we analyzed a disease-agnostic cohort of ~40,000 individuals to identify disease associations with SNPs in genes involved in the S1P pathway. RNA-seq data enabled comparison of key S1P-related genes in diabetic foot ulcer and non-ulcerated diabetic foot skin. For animal data, we infected euglycemic (EG) and hyperglycemic (HG) mice with MRSA and monitored infection resolution over 9 days. Biopsies were taken on days 1, 3, and 9, and S1P levels, lesion size, bacterial load, and cell death were assessed. To evaluate whether S1P can enhance clearance of dead cells/bacteria and promote healing, we treated mice with FTY720, an S1P agonist FDA-approved for multiple sclerosis RESULTS/ANTICIPATED RESULTS: PheWAS analysis suggests that SGPL1 SNP rs111439207 has protective effects against MRSA infection (OR = 1.71, P = 0.0004) and type 1 diabetes (OR = 1.325,P = 0.003). The RNA-seq dataset revealed increased SGPL1 expression (an enzyme responsible for S1P degradation) in the skin of diabetic patients with foot ulcers. In animals, we show that infected HG mice develop larger lesions, higher bacterial loads, and poor abscess formation. We found a correlation between dead cell buildup and a lower ratio of ingested dead cells in the skin by macrophages of HG mice compared to EG mice. Topical S1P treatment decreased lesion size and bacterial load in HG mice. DISCUSSION/SIGNIFICANCE OF IMPACT: Our data show increased expression of SGPL1 in diabetic patients. S1P deficiency during MRSA skin infection leads to tissue damage, uncontrolled bacterial growth, and poor resolution of the infection in mice. Topical treatment with S1P agonist is a promising therapeutic approach to enhance patient healing.

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The effect of providing genetic risk information on lifestyle behaviors in African Americans (linking GAINS)

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OBJECTIVES/GOALS: Linking GAINS evaluates a 14-week community-based program combining genomic testing, ancestry education, and culturally tailored nutrition to improve cardiometabolic health, literacy, and behavior among African American adults in Baton Rouge, Louisiana. METHODS/STUDY POPULATION: Sixty African American adults in Baton Rouge will be randomized into genetically blinded (GB) or unblinded (GU) groups. Both complete baseline surveys, biometric assessments, and a 14-week health behavior program with screenings, nutrition education, cooking classes, and exercise. The GU group receives Color Genomics testing and counseling at baseline; GB receives counseling post-intervention. Follow-up measures assess literacy, diet, and cardiometabolic outcomes. RESULTS/ANTICIPATED RESULTS: CHATGPT SAID: We anticipate improvements in genomic literacy, nutrition knowledge, and willingness to undergo genetic testing, particularly among the unblinded group. Participants are expected to adopt healthier eating and physical activity behaviors, leading to modest reductions in BMI and blood pressure and increased trust in genomics and preventive health research. DISCUSSION/SIGNIFICANCE OF IMPACT: Linking GAINS shows how combining genomic testing with culturally tailored nutrition education can improve literacy and lifestyle behaviors, offering a scalable model for advancing equitable precision health in African American communities.