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Community relationships in the dry skin microbiome

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Introduction: There is now increasing evidence that non-dry and dry skin show characteristic differences in the diversity and resilience of the skin microbiome. Resilience analysis based on the application of network co-occurrence techniques to microbiome data has in recent years proved a powerful tool in discriminating phenotypic and product induced changes in the skin microbiome. However, until now methodologies for the statistical comparison of such networks were lacking. Here we present a novel approach for the statistical comparison of resilience networks in the context of the skin microbiome associated with cosmetic dry skin.

Objective: To investigate the significance of changes in microbiome connectivity and fragility associated with dry skin and minimally/non-dry skin.

Methods: Healthy, female subjects with either moderately dry skin or non-dry skin on their lower legs provided informed consent to participate in IRB-approved studies. Samples were collected and processed for bacterial metataxonomic assessment using 16S rRNA gene sequencing. Analysis of microbial data using network co-occurrence modelling was undertaken and statistical comparisons made.

Results: Application of co-occurrence analysis to microbial taxa data indicates that the skin microbiome network of dry skin significantly altered relative to that of non-dry skin.

Conclusions: The microbiomes of dry and non-dry skin display significant differences in microbiome interaction and community resilience.

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Evaluating prebiotic effects of glycerol: Moving toward enhancing the care of infant skin

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Background: It is well accepted that infant skin barrier is more vulnerable than adult and that the microbiome plays a critical role in skin's natural defense. Therefore, it is important to nourish both the barrier and microbiome, to allow for their natural maturation. Glycerol is a humectant proven to hydrate skin. Previous in vitro studies have shown that glycerol can also be utilized by skin commensal bacteria as a food source, making glycerol a "skin prebiotic" ingredient.

Objective: The objective of this research was to examine the effects of glycerol on the skin microbiome in vivo.

Results: A double-blind, randomized, IRB-approved clinical study on volar forearms was conducted in healthy female adult subjects. Water or 10% glycerol in water were applied to test sites three times a day for five days under controlled conditions, followed by buffer extraction and analysis of lactic acid production. Lactic acid is known to have multiple skin benefits such as hydration, resilience and barrier function.

Conclusions: A robust increase in lactic acid production was observed following application of glycerol. This understanding can help inform future technologies to enhance infant skin care.

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Effect of concomitant medications on efficacy of sonidegib 200 mg daily in patients with locally advanced basal cell carcinoma: Results of the 42-month randomized, double-blind BOLT study

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Introduction: Sonidegib, a hedgehog pathway inhibitor, is approved for treatment of locally advanced basal cell carcinoma (laBCC) not amenable to surgery or radiotherapy. We present a post hoc analysis of the pivotal BOLT study that included objective response rate (ORR) and duration of response (DOR) per investigator review in laBCC patients receiving sonidegib 200 mg once daily (QD) also taking common concomitant medications.

Methods: BOLT was a randomized, double-blind, multicenter phase 2 study; patients were randomized 1:2 to sonidegib 200 or 800 mg orally qd, respectively. Tumor responses were assessed using modified Response Evaluation Criteria in Solid Tumors for laBCC. Safety assessments included adverse event (AE) monitoring.

Results: At 42 months, laBCC patients receiving sonidegib 200 mg qd (n = 66) achieved ORR (95% confidence interval [CI]) of 71.2% (58.7%-81.7%) by investigator review. The subpopulation receiving any concomitant medications (n = 37) exhibited ORR (95% CI) of 73.0% (55.9%-86.2%). ORR (95% CI) was 71.4% (29.0%-96.3%) for patients taking nonsteroidal anti-inflammatory drugs (NSAIDs; n = 7), 80.0% (44.4%-97.5%) for glucocorticoids (n = 10), and 88.9% (51.8%-99.7%) for salicylic acid and derivatives (SADs; n = 9). Overall median DOR (95% CI) was 15.7 (12.0-20.2) months. Median DOR was 13.6 months (95% CI not estimable [NE]) for patients on NSAIDs; 18.2 months (NE) for glucocorticoids; and NE for SADs. AEs were predominately grade 1-2, with grade 3-4 AEs related to sonidegib reported in 31.6% patients receiving 200 mg QD.

Conclusions: Common concomitant medications had no impact on efficacy in laBCC patients taking sonidegib 200 mg QD.

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Successful treatment of recalcitrant plaques and tumors in cutaneous T-cell lymphoma with combination intralesional 5-fluorouracil and topical imiquimod: A series of 8 patients

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Cutaneous T-cell lymphoma (CTCL) is generally regarded as an indolent form of cancer with treatments targeting management of symptoms and slowing progression rather than cure. While the majority of patients never develop extracutaneous disease, progression beyond the skin within 20 years of diagnosis can be up to 40%, depending on stage. Cutaneous lesions manifest as patches, plaques and tumors and the morphology and distribution of lesions largely drives treatment selection. Many patients experience a partial response to therapy and present with low density recalcitrant plaques and tumors. Regarding the use of topical 5% imiquimod for recalcitrant plaques, there are several case series, ranging from one to six patients, demonstrating complete response rates ranging from 50%-100% depending on study. Despite the well documented efficacy of intralesional 5-fluorouracil in nonmelanoma skin cancer, there are no reports of intralesional 5-fluorouracil as a treatment for CTCL. We present a case series of 8 patients with CTCL with recalcitrant thick plaques and tumors treated with combination intralesional 5-fluorouracil and topical imiquimod. A broad range of disease stages and phenotypes, including post-stem cell transplant recurrence and large cell transformed lesions were represented. Patients received between 1-5 injections 2 weeks apart of 5-fluorouracil with concomitant topical 5% imiquimod daily for a duration of 2 weeks to 3 months. Seven patients have achieved a complete response in index lesions, and one has had a good partial response after initial treatment with follow-up pending. This novel combination treatment is relatively inexpensive, well tolerated, and effective, warranting additional investigation.

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