Defining patterns of inflammatory marker expression associated with skin conditions

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A considerable proportion of presentations to hospitals involve inflammatory skin diseases (Stern 2012). A rash can be caused by drugs, allergies and infections. Adverse drug reactions are associated with 3.3-7.2% of hospital admissions, incurring considerable healthcare costs. Diagnosis relies on correlation of both clinical and histopathological findings but rashes are often difficult to differentiate, despite the available tests. This project investigates the possibility of rash diagnosis from an immunological perspective, by measuring cytokine and chemokine profiles within rashes (‘inflammatory signatures’).

Patients from PAH Dermatology received 2 mm punch biopsies of rash (‘lesional’) and nearby baseline (‘perilesional’) skin. Skin samples were homogenised in protease inhibitor solution and stored in -80°C. Inflammatory proteins were measured with Biolegend LEGENDplexTM bead-based immunoassay according to a panel based on previous literature associated cytokines with common inflammatory skin diseases. Data was visualised by using principal component analysis (PCA) and by generating heat maps.

Preliminary results

139 paired samples were collected. 58.4% male, 41.6% female; mean age 52.3 yrs.

Top 5 diagnoses: psoriasis (n=30), atopic dermatitis (n=19), hidradenitis suppurativa (n=12), cutaneous T-cell lymphoma (n=11) and drug eruption (n=10).

90.9% of patients were receiving anti-inflammatory treatment at the time of biopsy. We observe a cluster of psoriasis and atopic dermatitis signatures. On the other hand, psoriatic and lesional signatures are not clearly distinguished. Possible confounders include various effects of anti-inflammatory treatments and difficulty of obtaining baseline skin in diffuse rashes.

Figures 3 & 4: Heatmap with dendrogram and biplot of principal component analysis (PCA). Heatmap cells show colour-coded concentrations of analytes for each lesional sample according to diagnostic category. Dendrograms demonstrate a hierarchical clustering of correlated inflammatory signatures. In the PCA, samples located closely exhibit similar inflammatory signatures. Angles between vectors correspond to degree of correlation (>90° indicates negative correlation). PC1, PC2 = principal components 1 and 2.

Hypotheses and aims

We hypothesise that rashes may be distinguished by a detectable inflammatory marker pattern, or inflammatory signature, thus permitting the creation of a new diagnostic test to aid the physician.

Knowledge of inflammatory signatures may also inform the selection of targeted inflammatory treatments, thereby creating new avenues in the field of personalised medicine.

Aims:

1) Quantitate the presence of inflammatory proteins in the skin of patients with rashes
2) Define the correlation between inflammatory signatures and rash diagnosis

Conclusions and further considerations

This is a pilot study showing measurable differences in quantities of inflammatory markers in skin. Whilst differences between psoriatic and lesional skin are not clear, the preliminary analysis show clusters of psoriatic and eczematous inflammatory signatures.

Further investigation of the data set shall include: evaluation of perilesional skin as a baseline, consideration of anti-inflammatory treatment effects on the results, determining whether there is a general ‘rash’ signature and clustering according to expanded categorisations of rash.

Ethics and funding

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