PERSONALIZED MEDICINE

WHERE ARE WE IN ALLERGY (AND IN ECZEMA)?

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Personalized medicine, also termed precision medicine, is a medical procedure that separates patients into different groups— with medical decisions, practices, interventions and/or products being tailored to the individual patient based on their predicted response or risk of disease. The terms personalized medicine, precision medicine, stratified medicine and P4 medicine are used interchangeably to describe this concept, though some authors and organizations use these expressions separately to indicate particular nuances.

**Stratified medicine** Matching therapies with specific patient population characteristics using clinical biomarkers. (Trusheim et al, 2007)

**Precision medicine** Integration of molecular research with clinical data from individual patients to develop a more accurate molecular taxonomy of diseases that enhances diagnosis and treatment and tailors disease management to the individual characteristics of each patient. (US Nat Acad of Sciences report, 2011)

**P4 medicine** Clinical application of the tools and strategies of systems biology and medicine to quantify wellness and demystify disease for the well-being of an individual. (Hood, 2008)

**Personalised medicine** “Genomics+medical information technology+patient empowerment” (Millenson et al, 2006)
ALLERGY IS ALREADY PERSONALIZED MEDICINE

- IgE mediated (rhinitis, anaphylaxis, food allergy in young), anaphylactoid (ASA intolerance), delayed type allergy (contact allergy), immunocomplex mediated (drug exanthesas)
# Allergic Rhinitis Endotypes

<table>
<thead>
<tr>
<th>RHINITIS ENDOTYPES</th>
<th>NON-TYPE 2</th>
<th>TYPE 2</th>
<th>NEUROGENIC</th>
<th>EPITHELIUM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neutrophils</strong> IFN-γ IL-17 TNF</td>
<td>Eosinophils Mast cells ILC2 Specific IgE IL-5, IL-4/IL-13</td>
<td>Environment Life-style Microbiome Nasal anatomy</td>
<td>SP NK TRP channels</td>
<td>TSLP IL-33 Barrier / ciliary dysfunction Remodeling</td>
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<tr>
<td>COMMON COLD ACHIEV</td>
<td>Congestion Rhinorrhea Hyposmia Sneeze Itch NHR</td>
<td></td>
<td>GUSTATORY rhinitis</td>
<td></td>
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<tr>
<td><strong>RHINITIS PHENOTYPES</strong></td>
<td><strong>severity / duration / sensitization pattern / co-morbidities</strong></td>
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</tbody>
</table>

**Symptoms**

Nasal cavity: allergic rhinitis
FOOD ALLERGY ENDOTYPES

- Diagnosis
  - Characterize phenotype
    - Gender
    - Age
    - Race/ethnicity
    - Obesity
    - Environmental Exposure
    - Early vs. late onset
    - Atopic status
    - Refractory to therapy
  - Characterize Endotype
    - Biomarkers
      - Blood
      - Spinet
      - Saliva
    - Type 2 immune response
    - Non-type 2 immune response
  - Prognostic Biomarker
  - Tailored Therapy
  - Primary and Secondary Prevention
ATOPIC DERMATITIS ENDOTYPES

Potential endotypes for atopic dermatitis

- Non-lesional skin
- Acute disease flares
- Chronic remitting relapsing AD

Phenotype Endotype

PPEN

Th22 and Th17 driven inflammation

Type 2 immune response

Epithelial dysfunction

Th22 and Th1 driven inflammation

AGE

Lancet 387, 1109–1122, 12 March 2016
INCREASING KNOWLEDGE LEADS TO EVEN MORE ENDOTYPES
Shifting Towards Precision Medicine

Molecular fingerprinting → Big data analytics & Reference databases → Mobile information communication, technologies & precision medicine

Symptom-based medicine → Evidence-based medicine → Algorithm-based precision medicine
PRECISION MEDICINE IN FUTURE??

Can we act here for disease modifying strategy?

Disease severity

Clinical threshold

1. Screening BM at preclinical stage
2. Diagnostic BM
3. Predictive BM for response and/or adverse reaction to therapy
4. Severity BM
5. Prognostic BM for remission or chronicity

Subclinical disease  Clinically apparent disease  Remission  Cure
PERSONALIZED MEDICINE IN ATOPIC DERMATITIS – INDIVIDUAL PATIENT RESPONSE TO DUPILUMAB

~ 4/10 benefits

Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial.

~ 4/10 benefits
CONCLUSIONS

• Allergies and allergic diseases are highly diverse and all patients have their unique profile

• Incoming precision medicine brings high expectations and will ultimately benefit patients especially in developed world

• Individual responses to treatments should, as well as prevention and diagnostic approaches, be carefully taken into account in treating patient

• Patients are themselves best experts on their disease. They should be empowered and will become so, but at the same time, reciprocally, compliance to treatments and mutual decisions on factors affecting health should be strengthened