Molecular Epidemiology and OA biomarkers

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Molecular Epidemiology
Genetics osteoARtritis and Progression
The GARP study, baseline

- 188 sibling pairs + 4 trios
- OA; ACR criteria and radiographs
- Age: 60 yrs (range 43-79)
- Female: 82%

Inclusion:
≥ 2 joints OA

Familial background systemic factors
Genetics osteoARtritis and Progression
The GARP study, progression

Progression:
6 mths, 1 Y, 2 Y: 100 pairs
6 Y: 200 pairs

- ACR criteria and radiographs
- Questionnaires
- Urine / serum / blood RNA

Familial background fast progression
Course marker levels at timepoints
Genetic predisposition
Biochemical markers
The Garp study

**Blood**
- Osteocalcin → bone formation
- HsCRP → inflammation
- COMP → cartilage metabolism / turnover
- PIIANP → collagen synthesis

**Urine**
- u-CTXI → bone degradation
- u-CTXII → cartilage degradation
- TINE → cartilage degradation
- Glc-Gal-PYD → synovial tissue turnover
u-CTXII an OA biomarker?

GARP study. Cross Sectional. I. Meulenbelt

- Associated independently to ROA in hip, hand, facet and knee and composite score
- No association to discus degeneration (DD) of spine.

u-CTXII levels reflect whole-body cartilage degradation.

What if you did not measure OA at different joints. Elderly.

How specific is a marker for a joint
How realistic is such specificity

u-CTXII weakly associates to short term progression in GARP
Adjust for age. What is the relation with calendar/biological age.
### GARP study

Classification based on biomarker level; PCA analyses I. Meulenbelt

<table>
<thead>
<tr>
<th>Component</th>
<th>Effect</th>
<th>Joint</th>
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</thead>
<tbody>
<tr>
<td>Inflammation Local/systemic</td>
<td>HsCRP</td>
<td>Knee</td>
</tr>
<tr>
<td>Cartilage/bone metabolism</td>
<td>BMI u-CTXI Gly-Gal-Pyd OC</td>
<td>Hip</td>
</tr>
<tr>
<td>Age related changes</td>
<td>COMP PIIANP</td>
<td>Hand/Facet DD</td>
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What is the relation with calendar/biological age.
Can genetics help
The Garp study

Blood markers assessed

- Multiplex 17 cytokines / chemokines (Luminex)
- Thyroid levels
- Adipokines
- NMR spectra

Ex-vivo LPS stimulated cytokine levels (innate)

- IL-1β, IL-1Ra, IL-10

- Meulenbelt et al. Arthritis and Rheumatism
- Bos et al. (2009) Osteoarthritis and Cartilage 17:621-6