

## Towards a digital twin for osteoarthritis treatment

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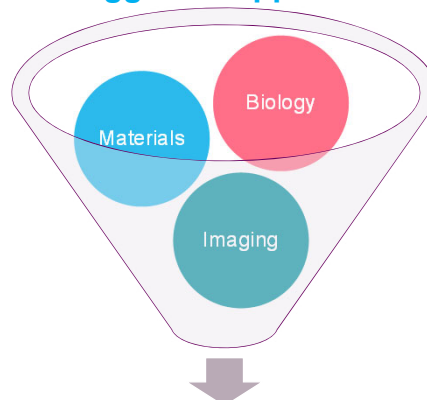


## The burden of osteoarthritis



- >300M individuals worldwide suffer from osteoarthritis
- No curative therapy: analgesics, total joint replacement
- Clear need for disease-modifying treatments and new biomaterials for tissue regeneration

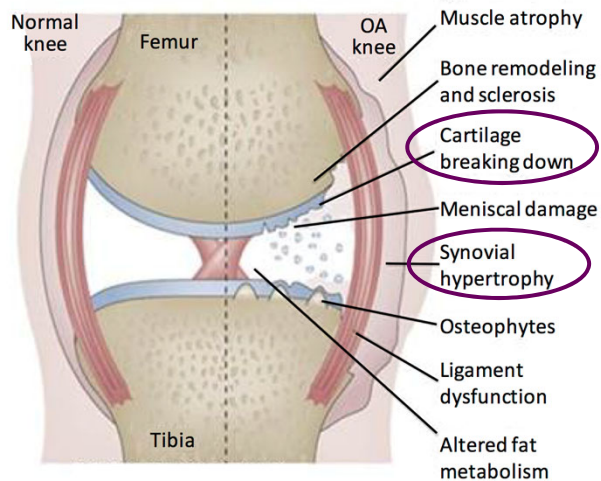
## Suggested approach



Better patient treatment

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## The hallmarks of osteoarthritis

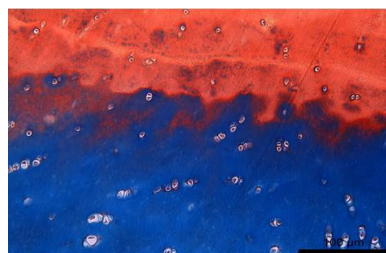
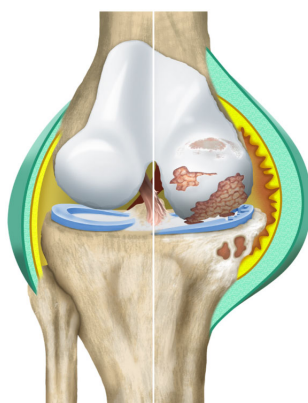


The underlying molecular mechanisms of osteoarthritis pathogenesis and progression remain incompletely characterised

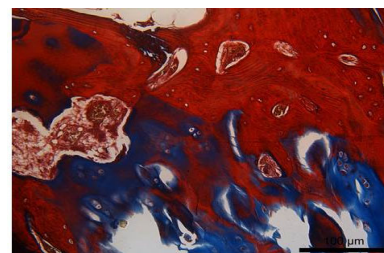
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## Cartilage degeneration



Intact cartilage

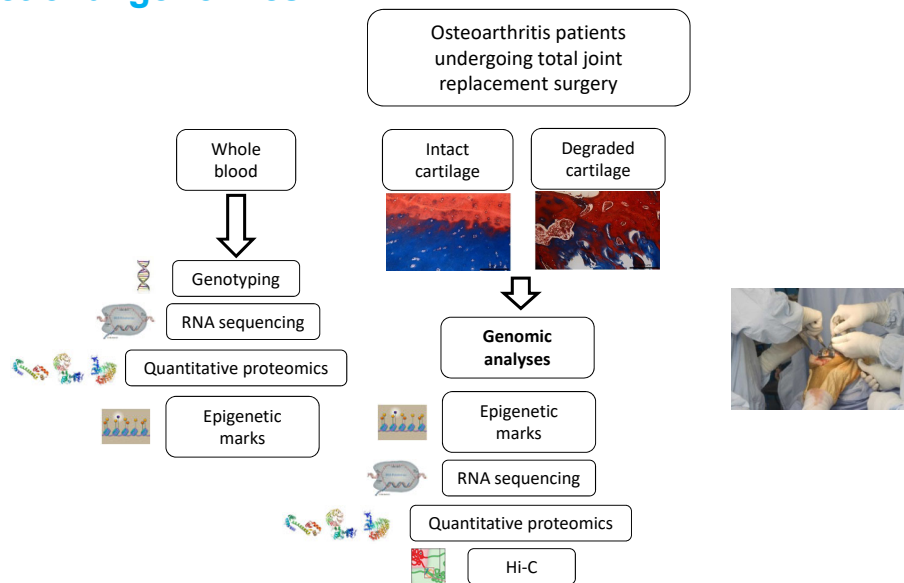


Degraded cartilage

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## Functional genomics



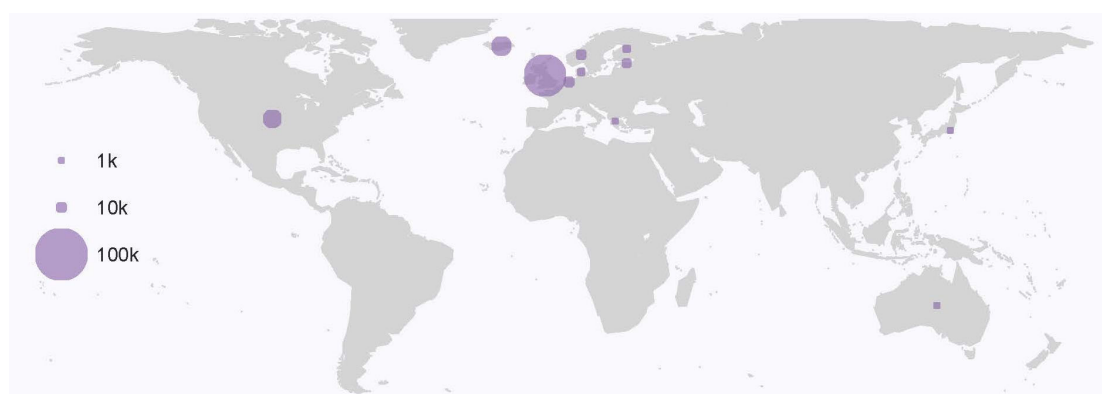
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## GO - Genetics of Osteoarthritis



180,000 cases, 1M controls

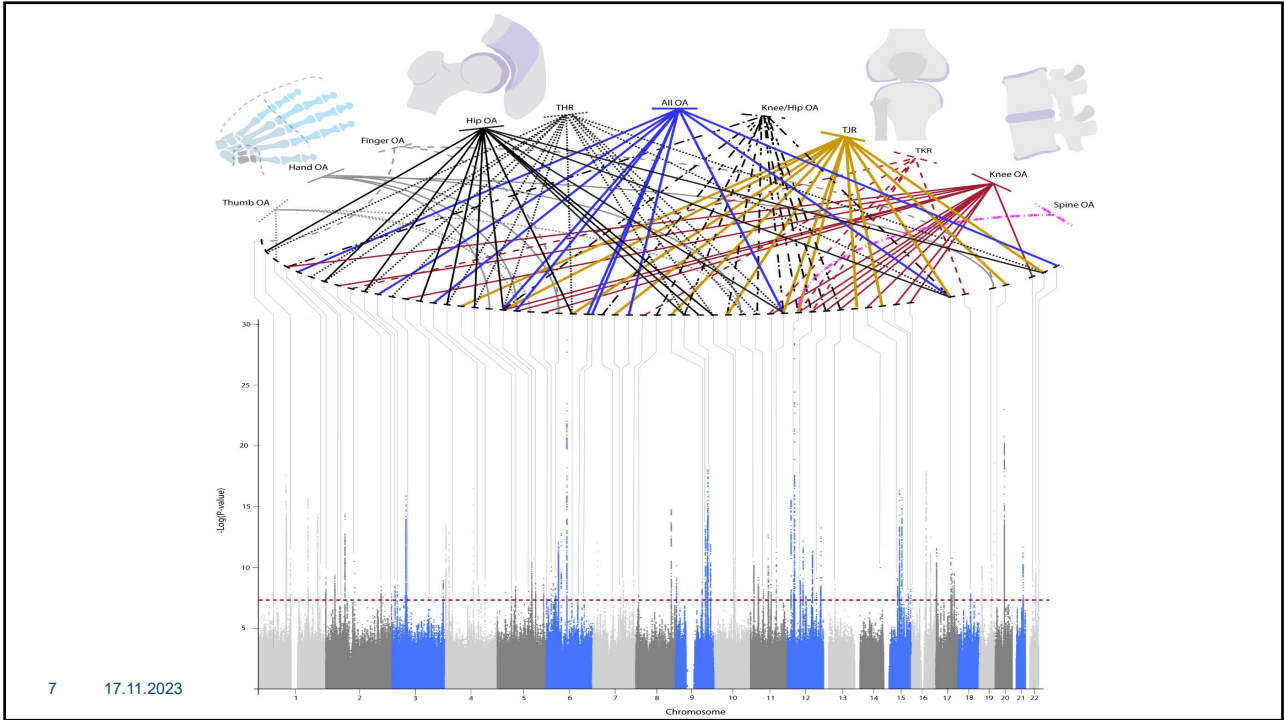
<https://www.genetics-osteoarthritis.com>

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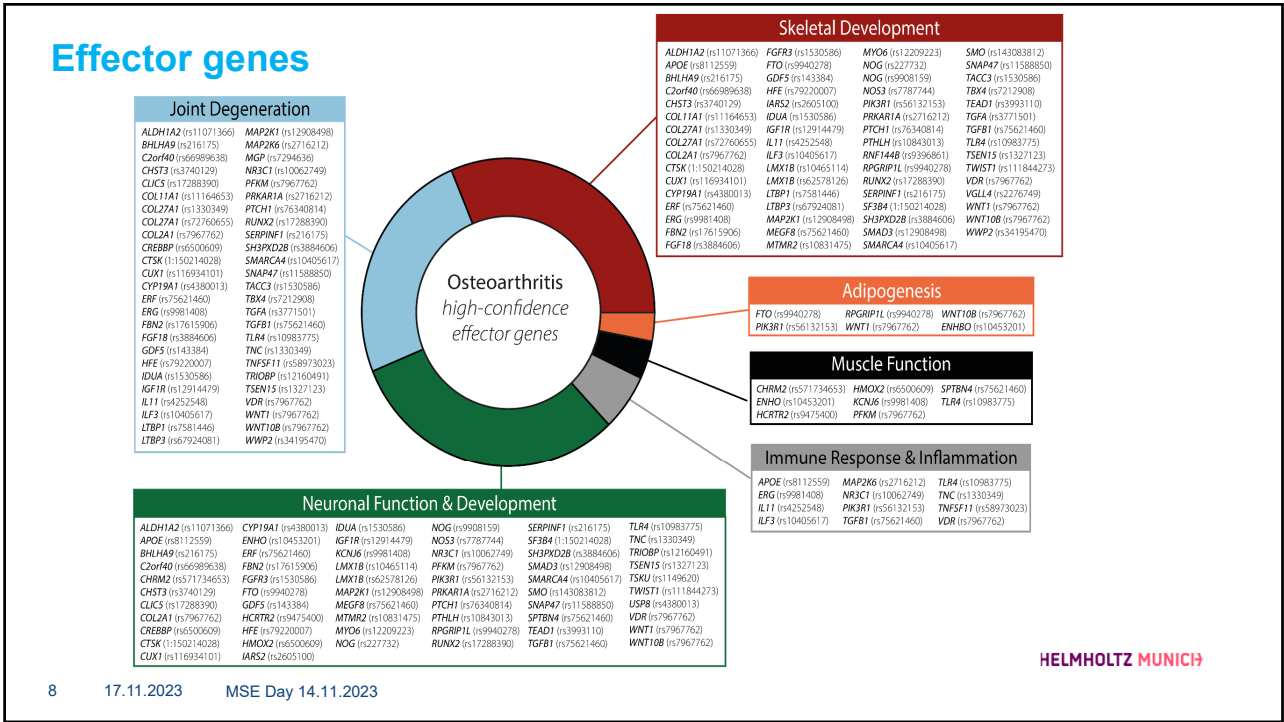
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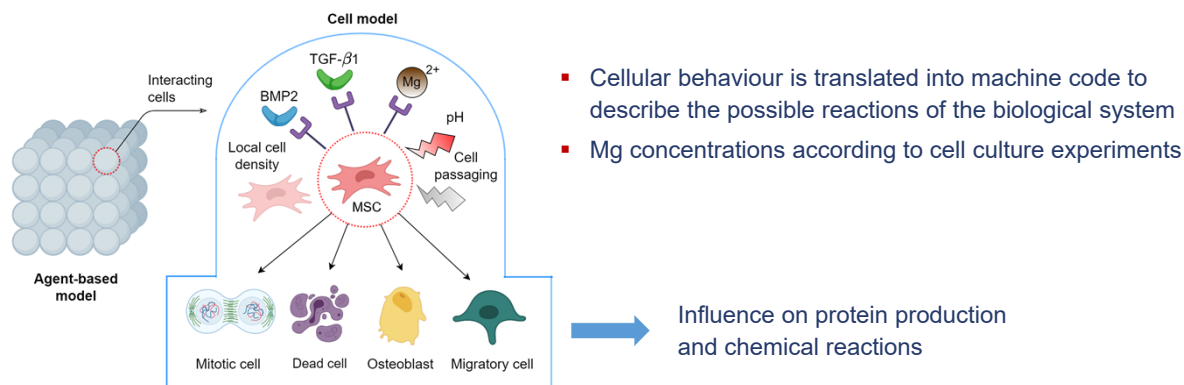


## Simulation of cell response for degrading Mg implants

### Fuzzy-agent based simulation of tissue regeneration

Mg is involved in more than 300 processes in cells.

- Obtain better biological understanding to specifically regenerate the tissue
- Finding the optimal concentration window = tailored degradation rate



MSC: Mesenchymal stem cells, BMP2, TGF- $\beta$ 1: signalling molecules

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Nourisa et al. Comp Struc Biotechnol J 19 (2021) 4110–4122



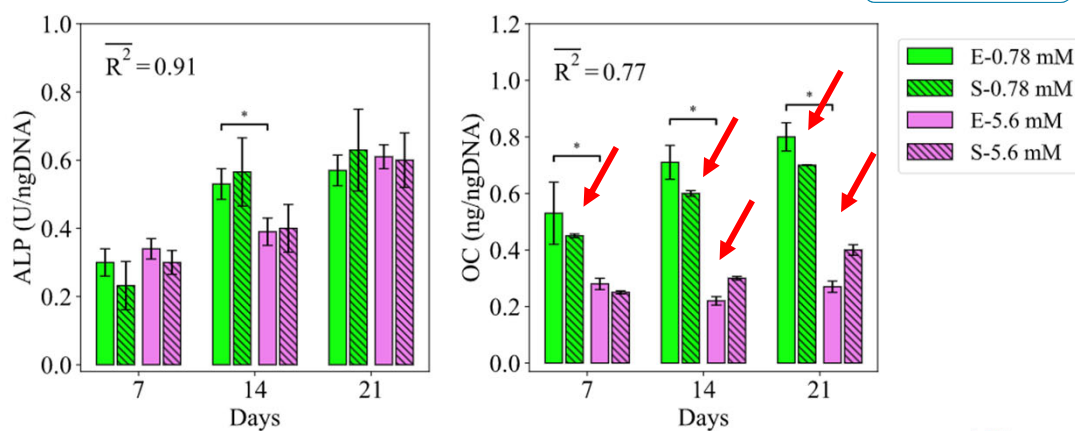
## Simulation of cell response for degrading Mg implants

### Production of ALP and OC – comparison of experiment and simulation

Different Mg concentrations and time points agree very well

**Better understanding  
Better targets**

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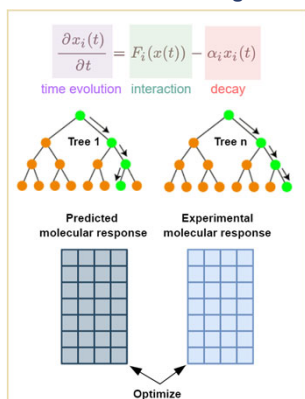
## Multimodal simulation of OA data obtained by HELMHOLTZ MUNICH

Multimodal data:

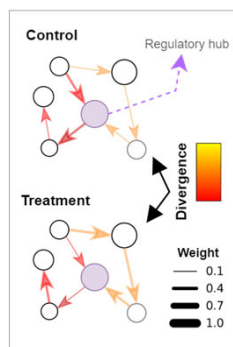
- ATAC-seq: chromatic accessibility
- mRNA-seq: gene expression

- Proteomics: protein level
- ChIP-seq: protein binding

Machine learning



Gene regulatory network



Identification of mechanism of action (MoA)

Digital replica: molecular response

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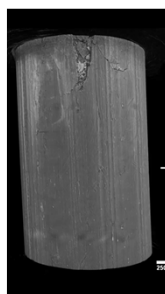
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## First steps to a biological digital twin for better material design

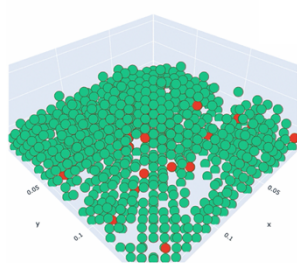
Material degradation - protein expression – tissue regeneration

Material degradation



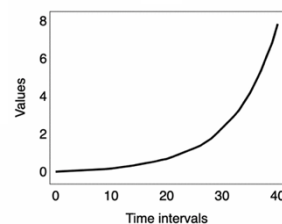
Dynamic Mg concentrations

Cell response

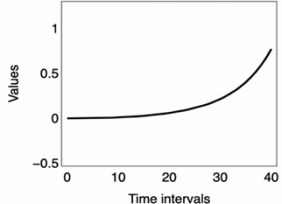


Green: living MSC  
Red: dead cells

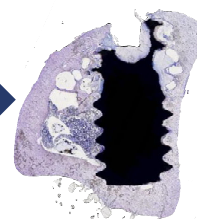
TGF - Transforming growth factor



BMP - Bone morphogenetic proteins



Tissue regeneration



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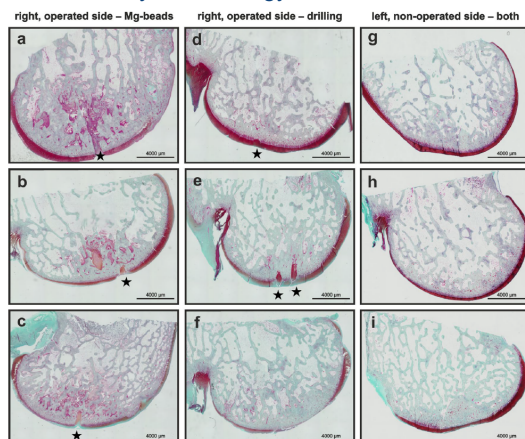
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## Bringing together treatment and diagnostics

### How to characterize cartilage quality?

#### Current analysis: histology



Angrisani et al. eCM 42 (2021) 179-195, DOI: 10.22203/eCM.v042a14

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#### Examination of cartilage: state of the art

- Invasive mechanical probing
- Histological analysis (*post mortem* / *ex vivo*)
- Not suitable for early diagnosis at large scale
- Limited applicability in longitudinal monitoring (e.g., during implant development / therapy)

#### Key scientific question

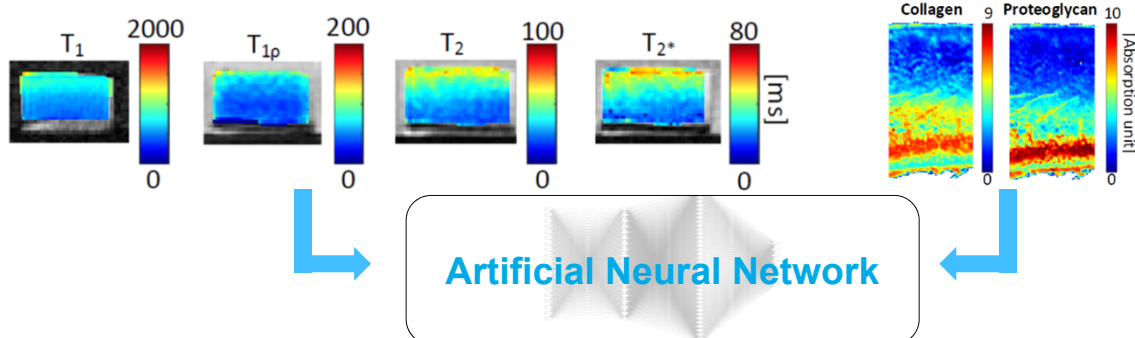
- How to quantify mechanical properties of cartilage non-invasively *in vivo*?



## Bringing together treatment and diagnostics

### Non-invasive AI-based diagnosis

- Collect multi-contrast quantitative MRI data



- Train artificial neural network (ANN) to extract from multi-contrast MRI data composition and mechanical properties non-invasively
- Support treatment by non-invasive early diagnosis and longitudinal monitoring

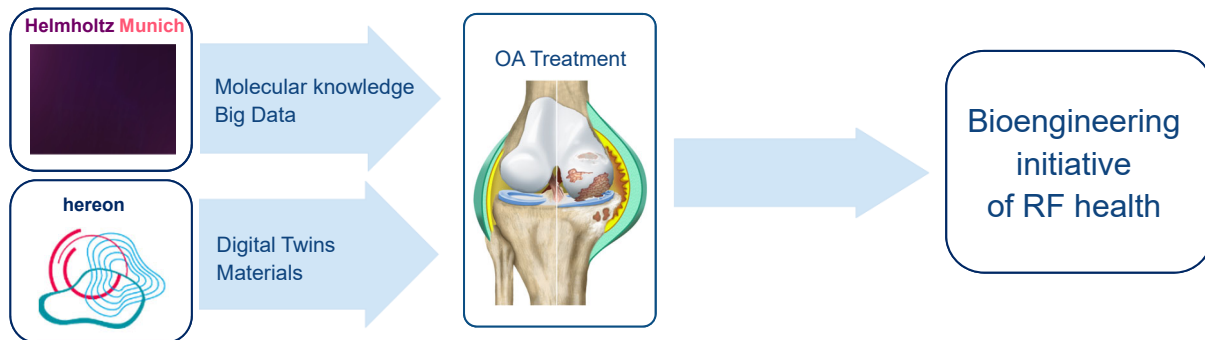
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## Conclusions

Merging RF-fields expertise for treatment optimization



**Thank you!**