



# IMMOSCAN

The role of IMMune OSteoclasts in CANcer – implications for therapy

*Claudine Blin, Hanna Taipaleenmäki, Anna Teti, Dominique Heymann, Thomas L Andersen*



# Primary and metastatic bone tumors



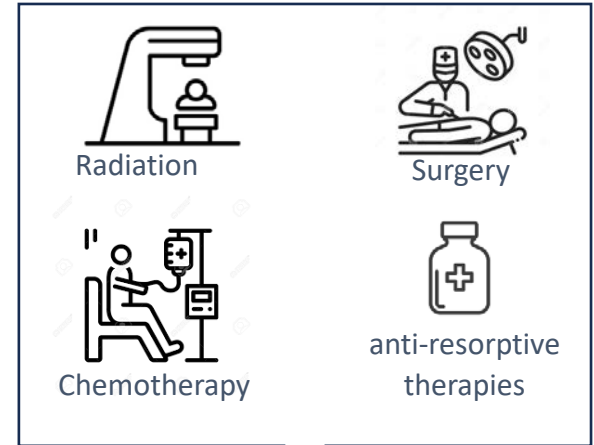
## Osteosarcoma

- Transformed osteoblasts produce osteoid matrix
- Para-tumor osteolysis
- 5 year survival:
  - 78% for localized disease
  - 20% when metastatic



## Breast cancer bone metastasis

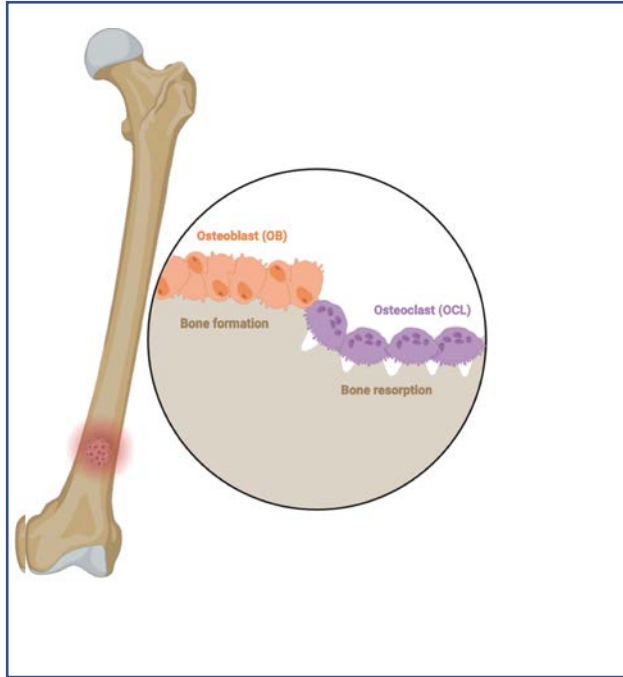
- osteolysis promoting tumor growth and dissemination
- incurable disease:
  - median survival 20 months



∨ tumor growth  
∨ bone destruction  
but no cure of the disease

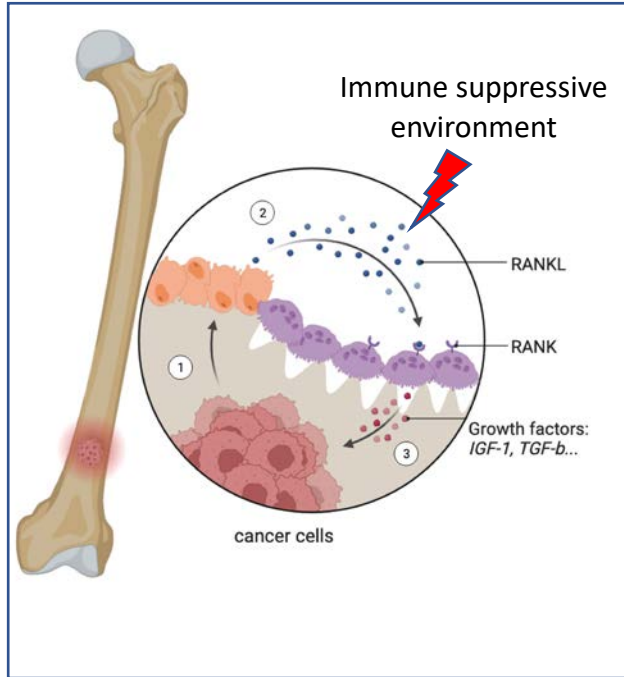
# *The bone marrow environment: the key role of osteoclasts*

## The vicious cycle

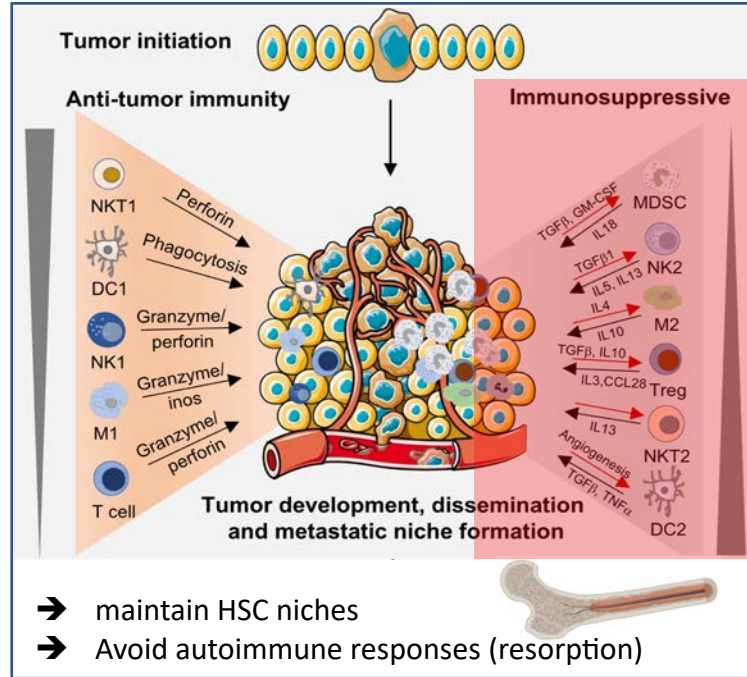


# The bone marrow environment: the key role of osteoclasts

## The vicious cycle

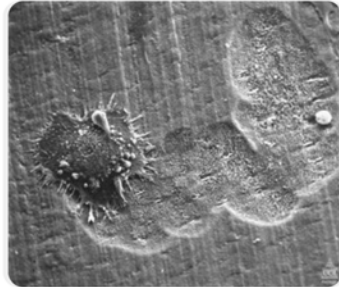
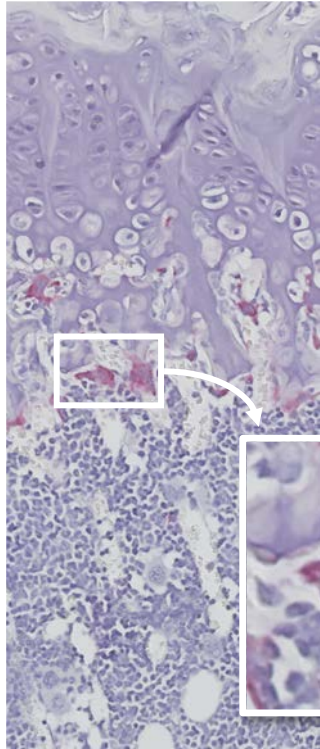


## Immune suppressive environment



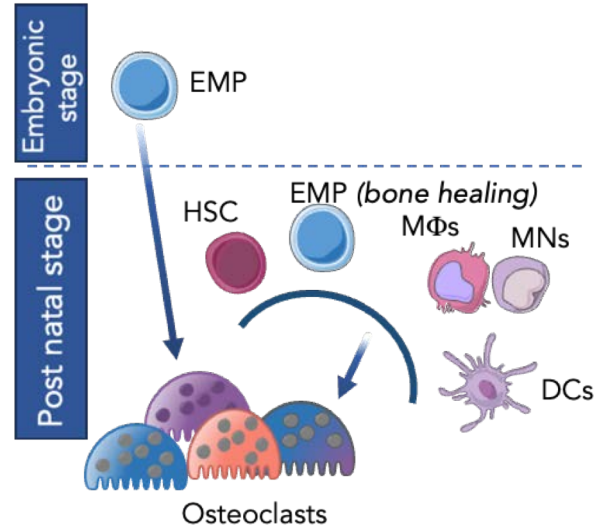
# Osteoclasts

Multinucleated bone-resorbing cells...



From A Boyde, boneresearchsociety.org

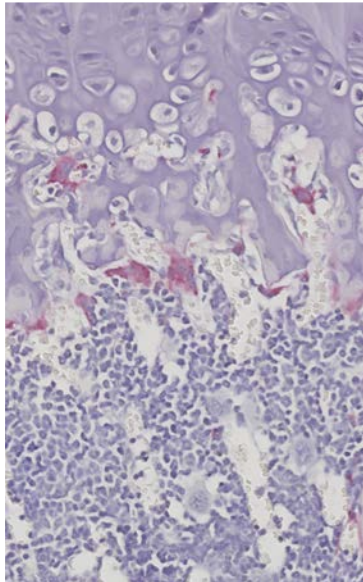
... and myeloid cells endowed with an innate immune function



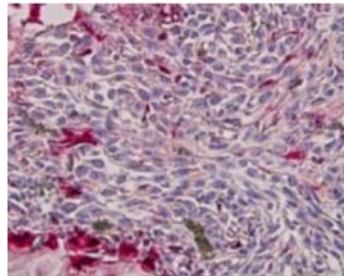
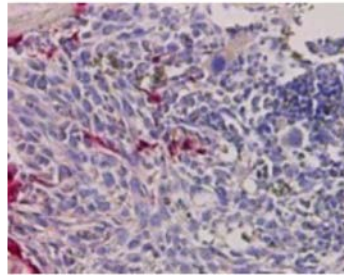
# *Osteoclasts in bone tumor and metastasis*

## **Mouse**

Control

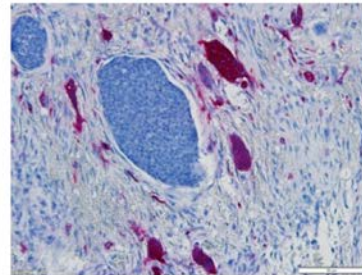


Breast cancer  
bone metastasis

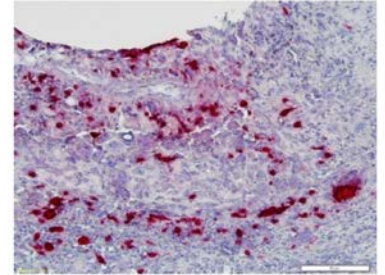


## **Patients**

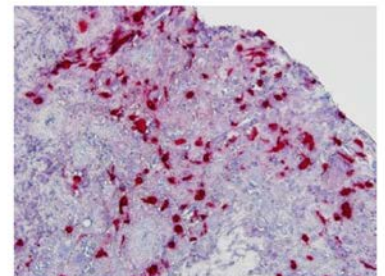
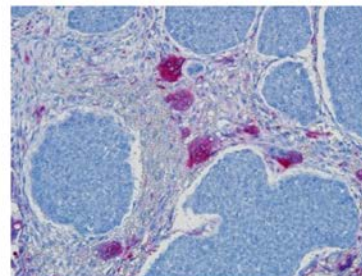
Breast cancer  
bone metastasis



Osteosarcoma

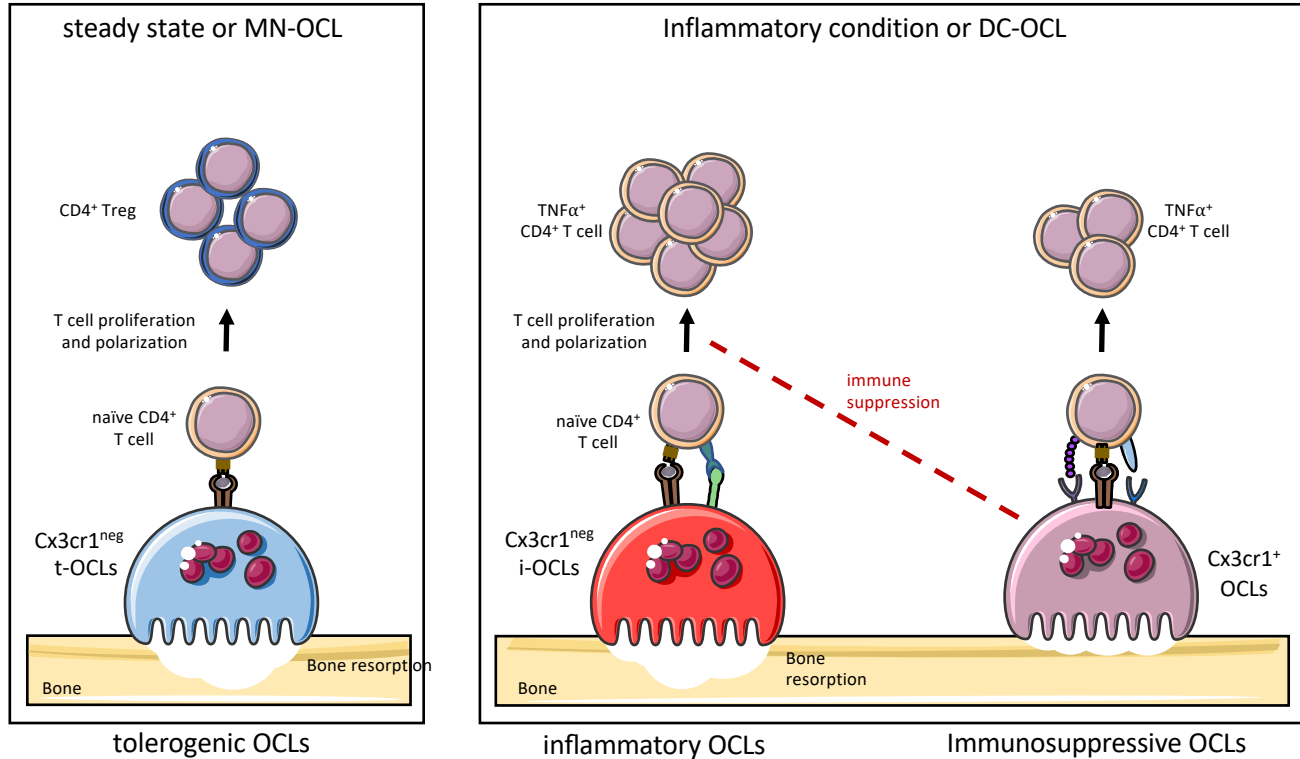


TRAP activity



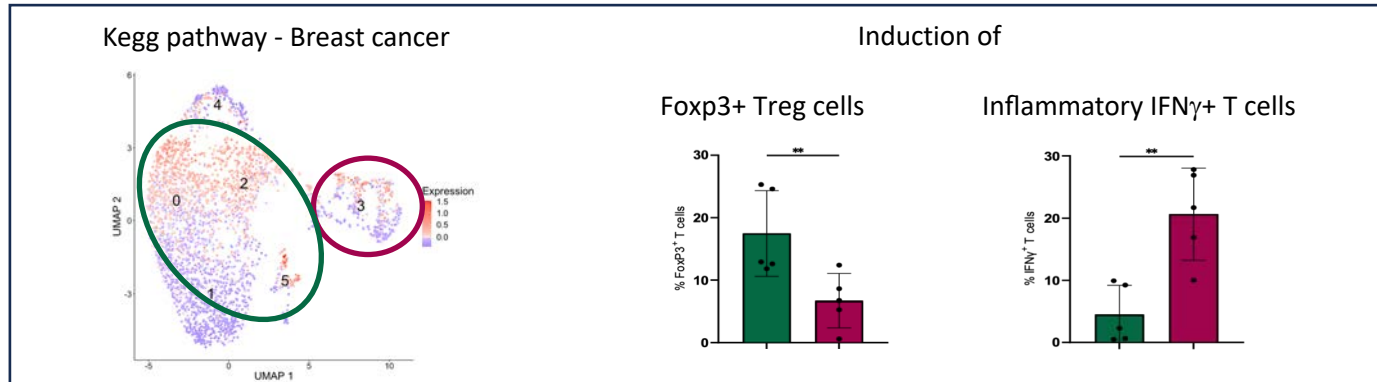
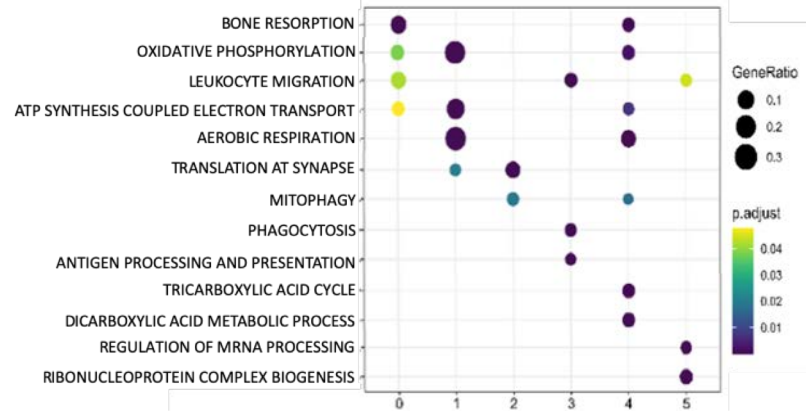
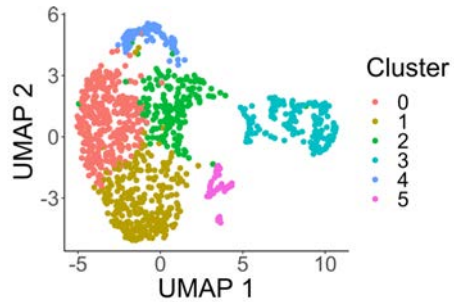


# The immune functions of osteoclasts



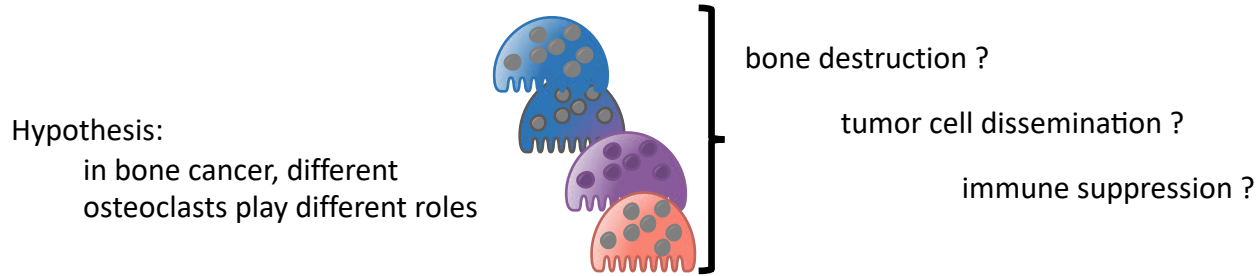
# Osteoclasts diversity in normal mouse

scRNAseq on OCL from healthy mice





# Hypothesis and aims



Global aim : Characterize osteoclasts in the context of bone tumor and metastasis in mouse and patients

AIM 1

- Identify and characterize OCs in bone cancer

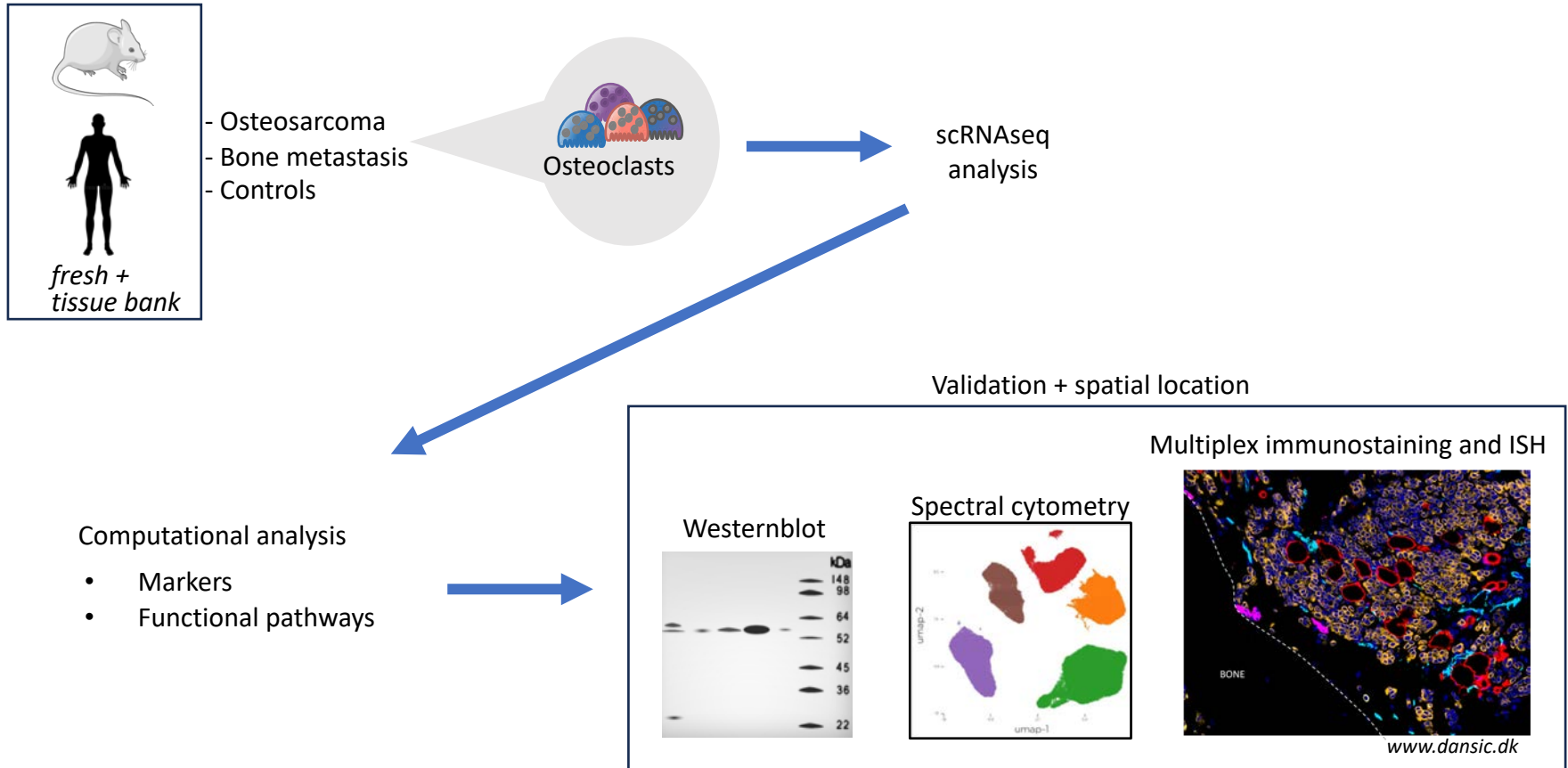
AIM 2

- Determine the origin, function and molecular mechanism of immune OCs

AIM 3

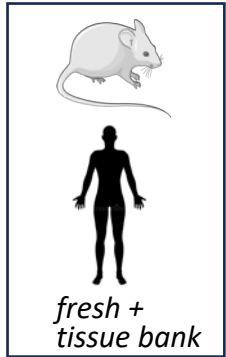
- Target the immune OCs to improve the efficacy of immunotherapy

# AIM 1. identify and characterize OCs in bone cancer



# AIM 2. origin, function and molecular mechanism of immune OCs

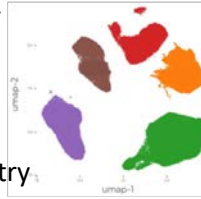
Blood  
Bone marrow



- Osteosarcoma
- Bone metastasis
- Controls

## Identify progenitor of immune OCs

Phenotyping of  
myeloid cells



in vitro OC differentiation assay +  
phenotyping of immune OCs

## Pathway validation and modulation

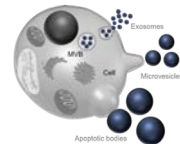
In vitro assays

- immune function
- immune suppression
- bone resorption
- -----

Modulation of the most relevant pathways

- pharmacological inhibitors
- siRNA
- Crispr/Cas9

## Role of OC extracellular vesicles



Phenotyping

Role in immune suppression  
(in vitro/in vivo assays)

### AIM 3. Target immune OCs to improve the efficacy of immunotherapy



#### Target immunosuppressive OCs in vivo

- immune evasion / check points
- Most promising pathways



- Tumor growth
- Bone status
- Immune status

#### Evaluate prognosis markers in the blood



- EV
- % progenitors of immune OC

- Osteosarcoma
- Bone metastasis
- Controls



#### Analyze published datasets from patient cohortes



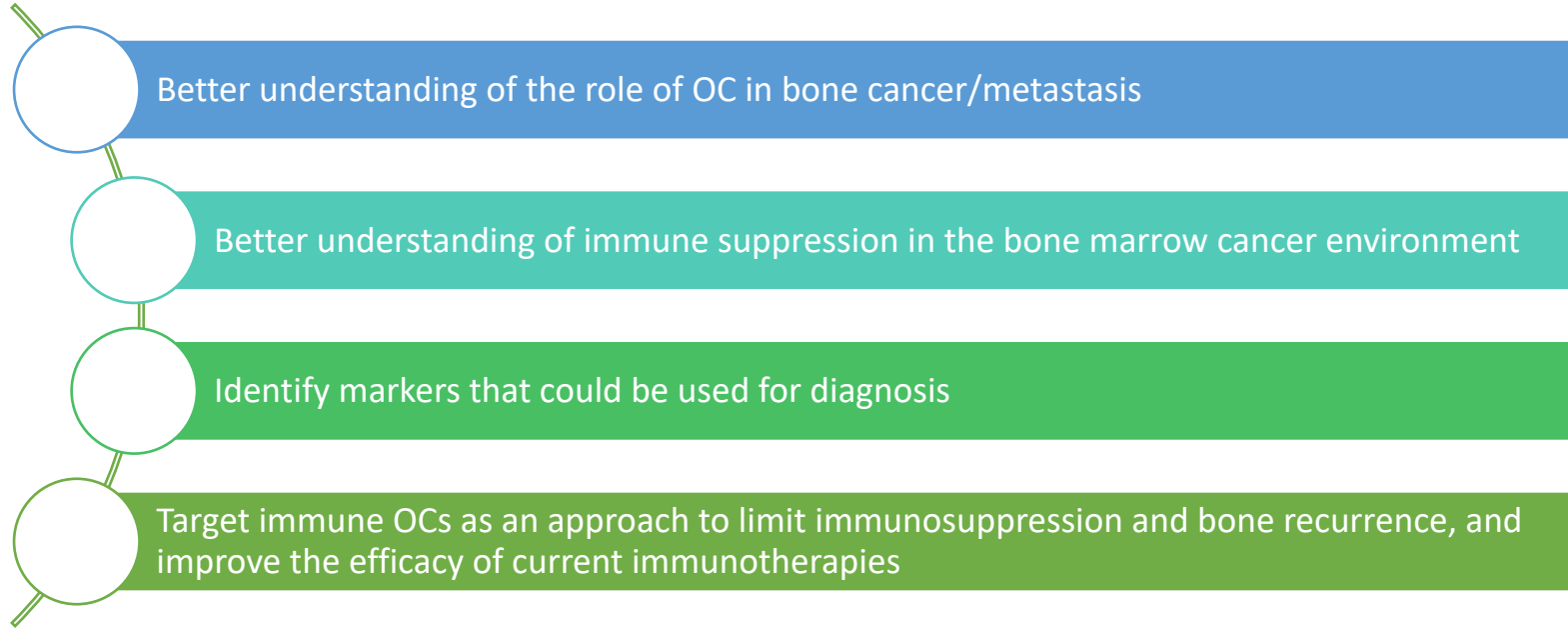
Correlate markers of immune OCs with bone relapse and survival

#### Evaluate prognosis markers in the blood



correlation with cancer type and disease stage:  
proof-of-concept analysis of diagnostic relevance

## *Expected results and perspectives*



# Consortium



Coordinator

**Hanna Taipaleenmäki**  
(Munich, Germany)

- Bone oncology
- Bone tumor environment
- Interaction bone/cancer cells



**Dominique Heymann**  
(Nantes, France)

- Osteosarcoma
- Bone tumor environment
- Bone pathophysiology



**Anna Teti**  
(L'Aquila, Italy)

- Bone pathophysiology
- Osteoclast biology
- Role of EV in bone



**Claudine Blin**  
(Nice, France)

- Osteoclast diversity and immune function
- Osteoclast origin
- Osteoimmunology



**Thomas L Andersen**  
(Odense, Denmark)

- Bone tumor /metastasis
- Bone imaging
- bone surface – bone marrow interface

*Amy Ribet*



*Australia*

*Daria Klusa*



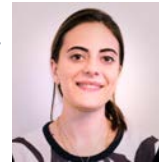
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*Maria Materozzi*



*Italy*