# Bone Tissue Engineering: Scaffolds, Factors, and Cells


**Yusuf Khan, Ph.D.**

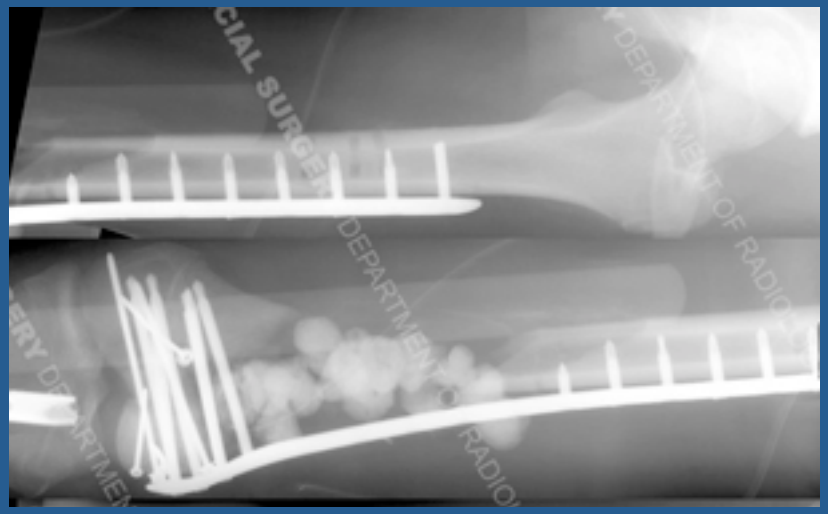
**Institute for Regenerative Engineering**
**New England Musculoskeletal Institute, Dept. of Orthopaedic Surgery**
**University of Connecticut Health Center, Farmington CT**

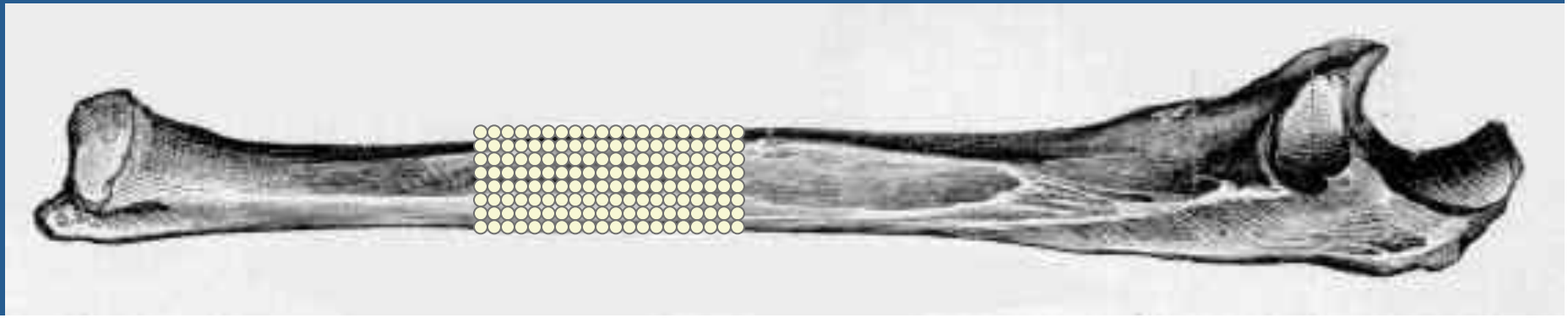
# Bone Grafting: Autograft vs. Allograft

- **Gold standard for bone graft procedures**
- **Osteogenic, osteoconductive and osteoinductive**
- Limited supply
- Donor-site morbidity
- Post-operative pain and infection

- **No donor site morbidity**
- **Reduced surgical time with no secondary surgery**
- **Fewer supply limitations/considerations**
- Immunorejection
- Reduced functional capacity
- Non-Unions
- Poor-bone allograft incorporation

# Long Bone Segmental Defect





# Bone

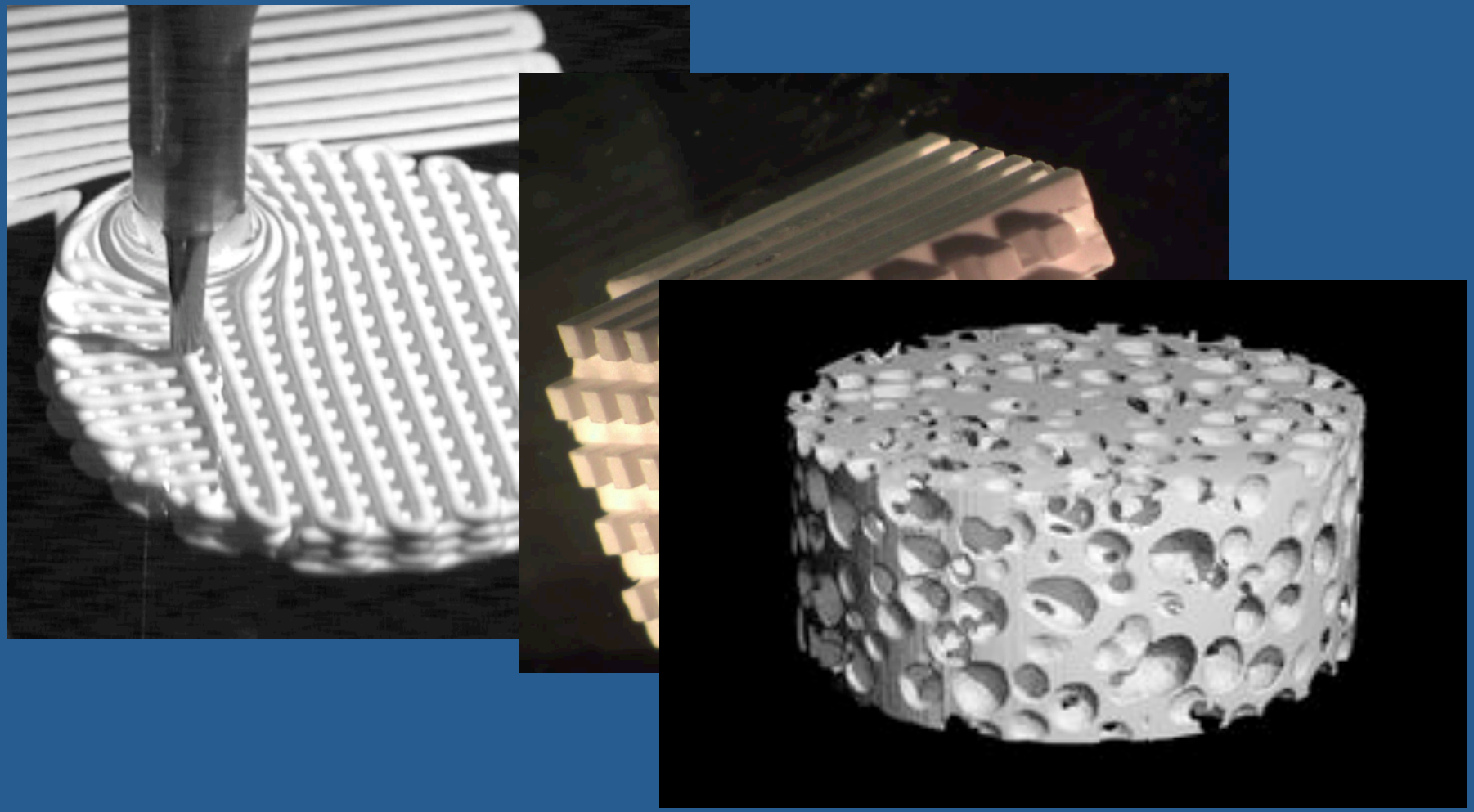
# Materials used in Scaffold Development

- Natural Materials
  - Collagen
  - Hyaluronic acid
  - Chitosan
- Synthetic Materials
  - Poly(ε-caprolactone)
  - Poly(anhydrides)
  - Polycarbonates
  - Polyesters
    - Polylactide
    - Polyglycolide
    - Poly(lactide-*co*-glycolide)

# Parameters for a Suitable Scaffold

- Biocompatible – no/minimal inflammatory or immune response
- Biodegradable – fully resorbed or degraded by body to allow complete healing
- Biomechanically sound - provides appropriate mechanical properties for support
- Osteoconductive - allows cells to attach and migrate
- Osteointegrative – good bond at material/bone interface
- Easily formed and manipulated

# Scaffold Choice

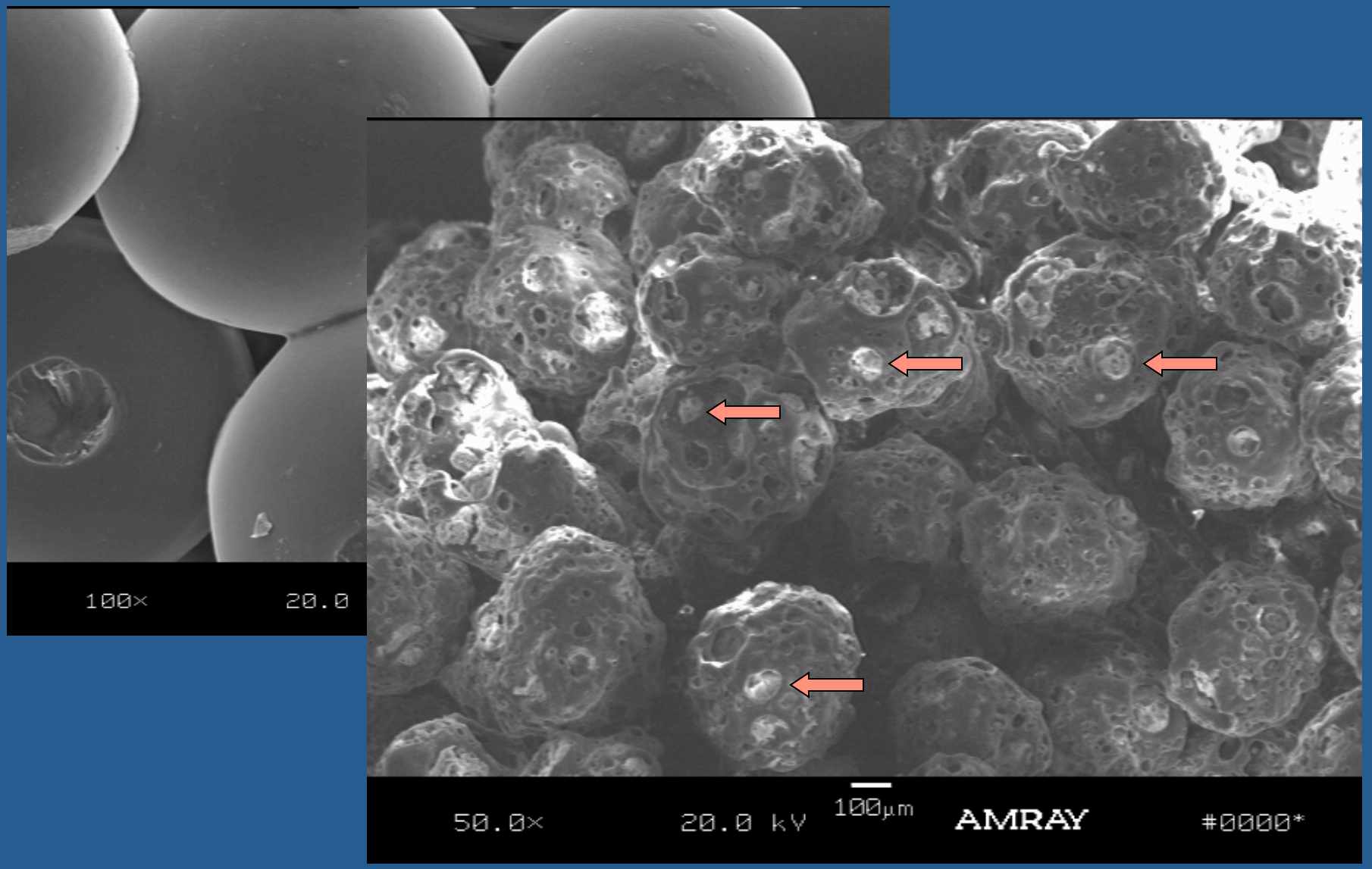


http://www.biomech.ethz.ch/research/muller_group/ste/#scaffolds

http://www.bjb.engr.wisc.edu/Research/Completed%20Projects/bone_scaffolds/bone_scaffolds.html

https://wiki.engr.illinois.edu/display/BIOE414/Team+5+Domo+Arigato,+micro-Roboto+%28Deposition%29

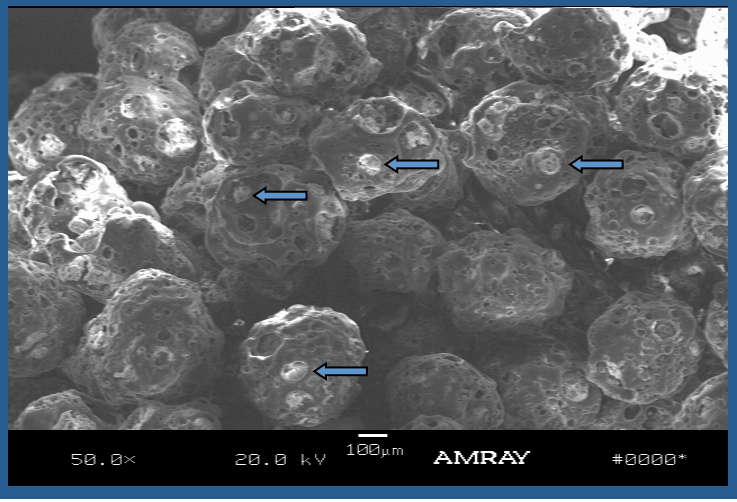
# Sintered Polymeric Microspheres



# Candidate Materials

**POLYMER (PLAGA)**
Strength, formability, ease of use, biodegradable
Limited osteoconductivity, osteogenicity and bioactivity

**CERAMIC (CaP)**
Bioactive, osteointegrative, osteoconductive
Brittle in failure, poor formability, slow degradation




**POLYMER/CERAMIC COMPOSITE**
Biodegradable, formable, osteoconductive, osteointegrative material

# Growth Factors

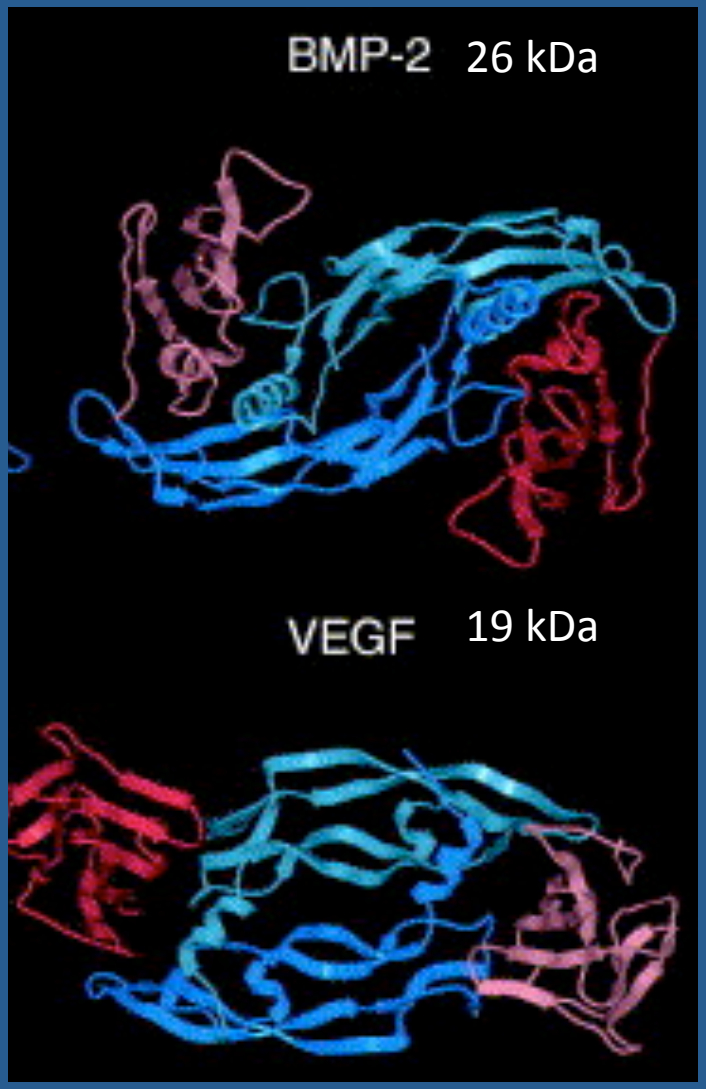
Bone Morphogenetic Proteins (BMP-2)

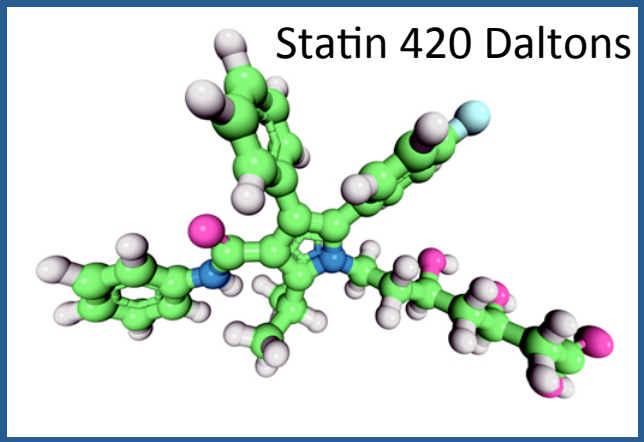
- **Dr. Marshall Urist, 1965**
- **Subgroup of TGF-β family**
- **Widely studied, highly effective in inducing bone formation**
- **FDA approved for certain orthopaedic applications**

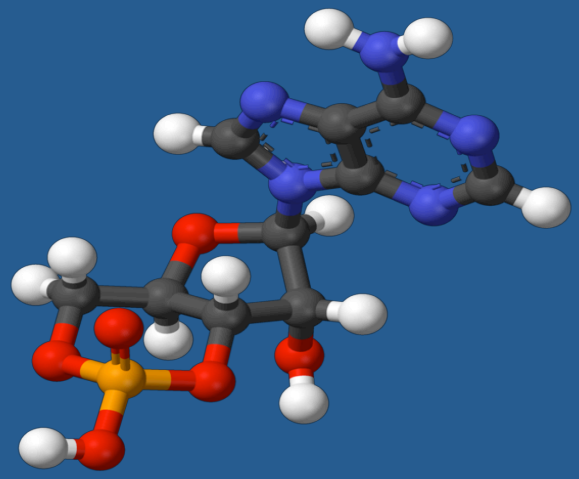
Vascular Endothelial Growth Factor (VEGF)

- **Produced by osteoblasts, tumor cells, others**
- **Recruits endothelial cells for vessel formation**
- **Induces proliferation of endothelial cells**
- **Enhances osteoblast differentiation**

# Small Molecule Delivery



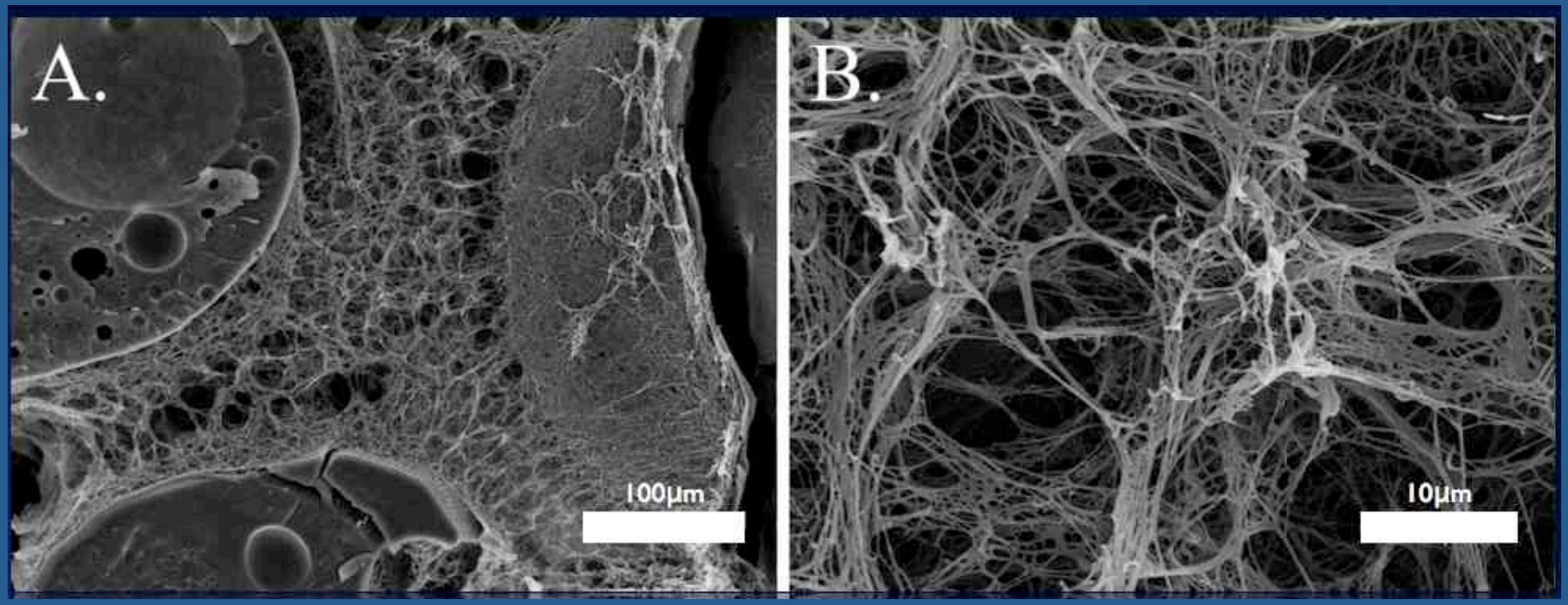



**Cyclic AMP 329 Daltons**

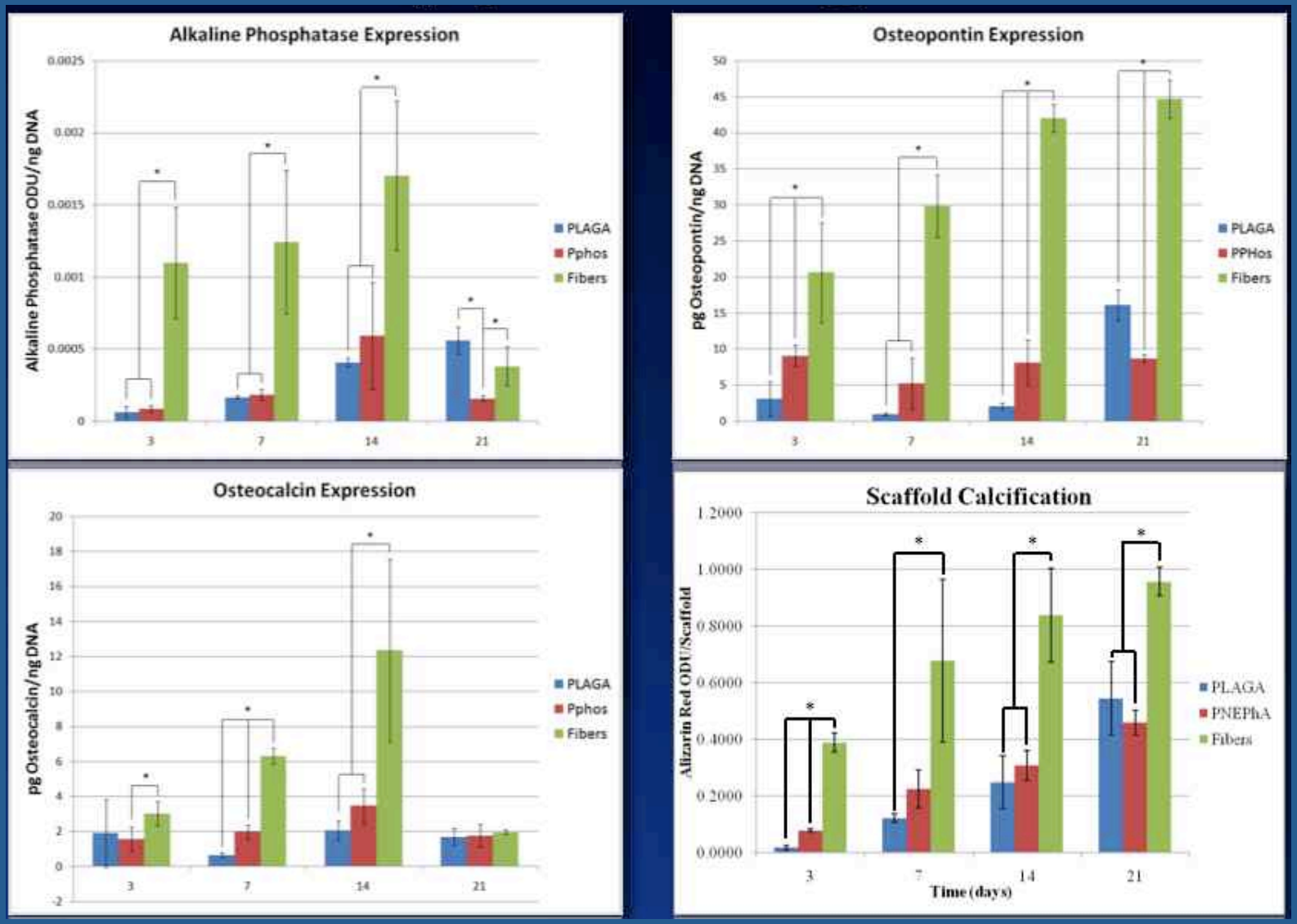
# Cells

- Cells play key role in bone regeneration
- Unclear whether cells should be added or recruited
- Designing scaffolds to influence cell behavior
  - Works in conjunction with growth factors

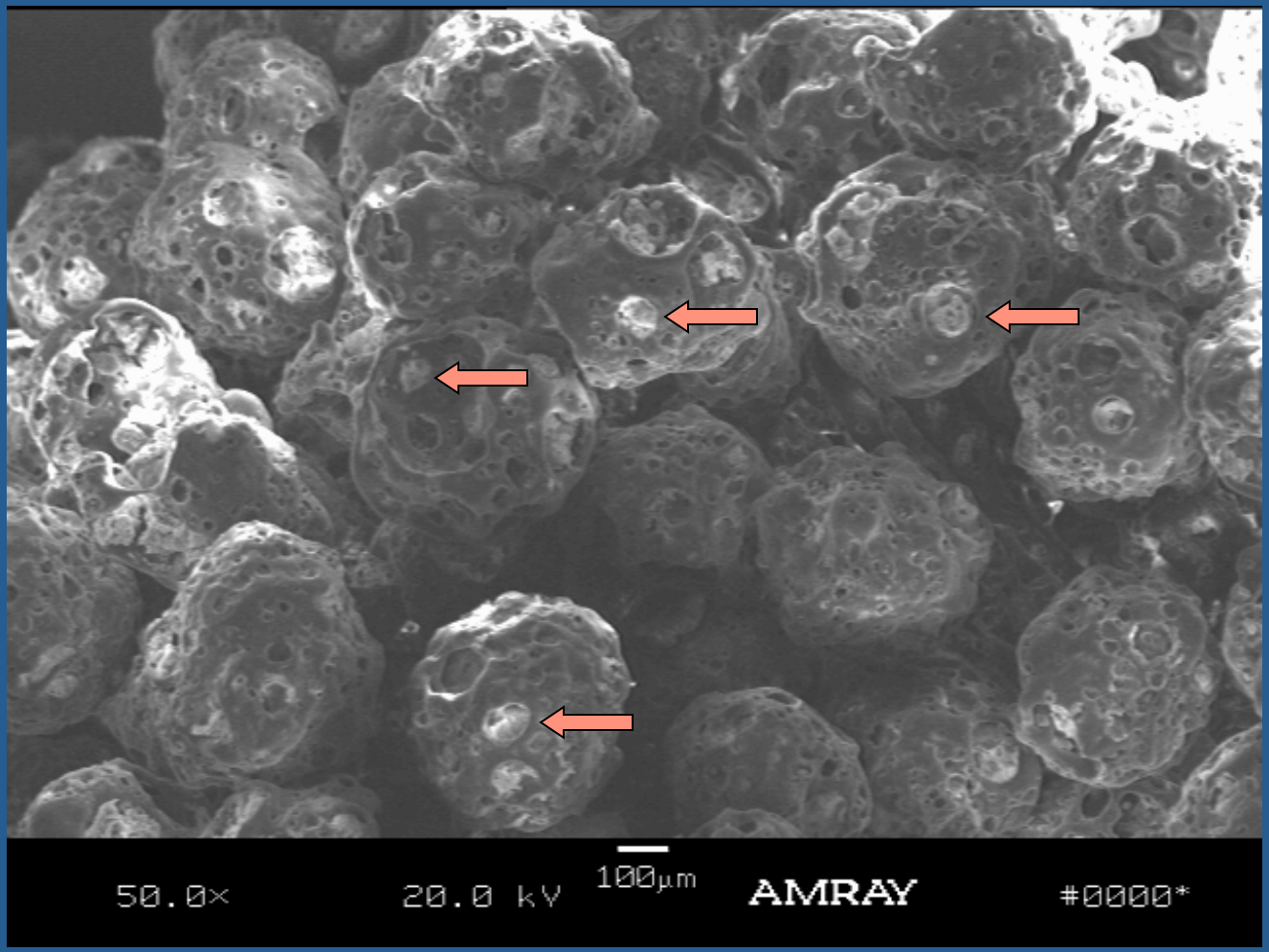
# Synthetic ECM in Pore Spaces



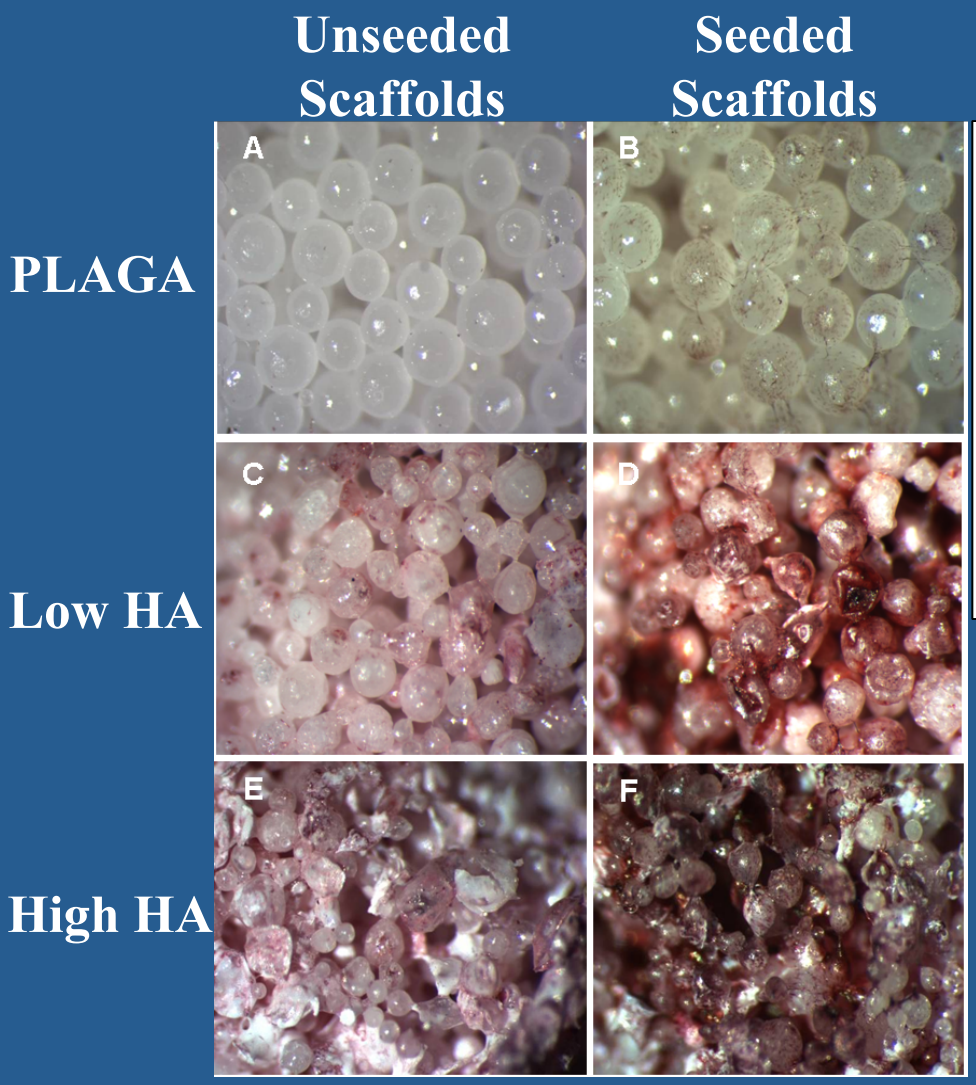
# Cellular Response to Nanofibers

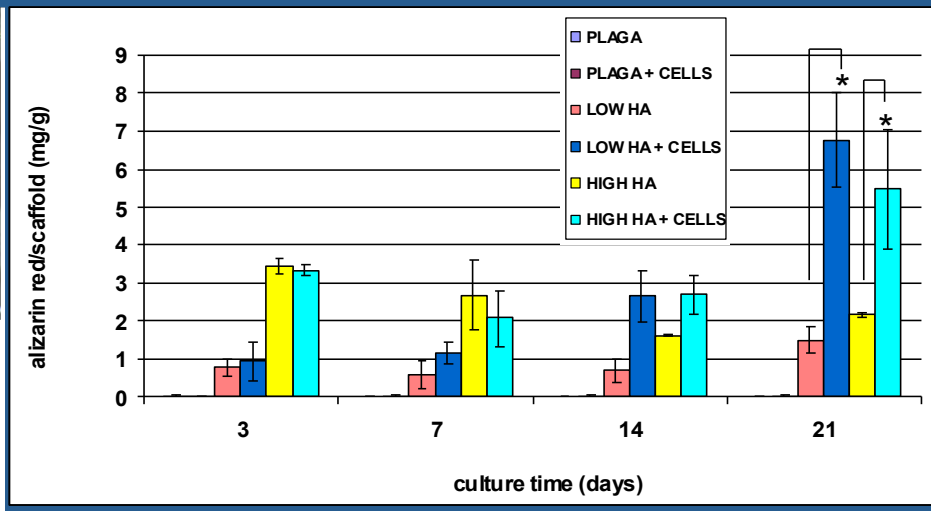


# Composite Microspheres

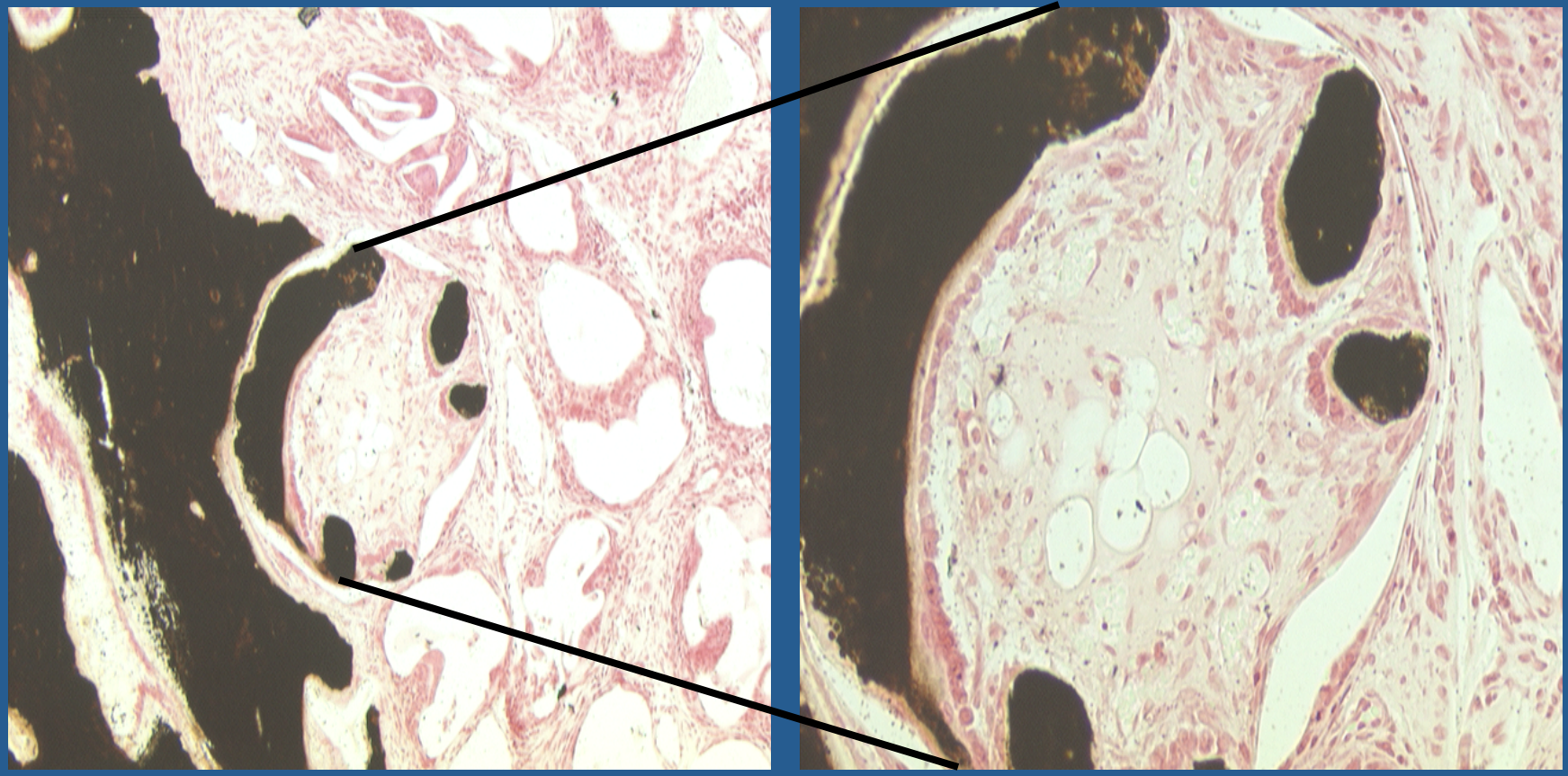


# In Vitro Mineralization



# In Vivo Data



# Summary

- Scaffolds
  - Broad goal is to have porous, interconnected structure with mechanical integrity
  - Achievable through multiple strategies
- Growth Factors
  - Can render scaffolds osteoinductive
  - Large molecules more challenging than small
  - Work under way to find effective small molecules
- Cells
  - Key component of successful healing
  - Susceptible to molecular, mechanical, and architectural influences