The State of Fibrous Dysplasia/McCune-Albright Syndrome Research

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Fibrous dysplasia /McCune-Albright Syndrome

Skeleton
- Craniofacial
- Axial
- Appendicular

Extra-skeleton
- Endocrine
  - thyroid
  - precocious puberty
- Skin
- Others
What causes FD/MAS?

- Gene: **GNAS**
- Protein: \(G\alpha_s\)
- Cells
- Tissue
What does $G\alpha_s$ do:
It is a master regulator of cell activity;
an “on and off switch”

- Skin
  - Café-au-lait
    - precocious puberty
- Ovary
  - fibrous dysplasia
    - hyperthyroidism
- Bone
- Thyroid
  - growth hormone excess
- Pituitary

Others: pancreas, heart, brain, etc.
The cells that make bone: skeletal stem cells, mesenchymal stem cells

- Stem cell
- Bone cells
- Osteoblast
- Osteocyte
- Cartilage cells (chondrocytes)
- Fat cells (adipocytes)
- Helps make blood cells (hematopoietic support)
Effects of $\text{G}_{\alpha_s}$ mutation in bone stem cells

- Abnormal bone cells
- Osteoblast
- Osteocyte
- Cartilage cells (chondrocytes)
- Fat cells (adipocytes)
- Stem cell

Helps make blood cells (hematopoietic support)
Affected tissues in FD/MAS
a somatic, mosaic condition

the “map” of affected tissues is charted in utero
What are the effects of in utero “mapping”?  
Affected bones appear early

n = 109 subjects, 266 bone scans, f/u up to 32 y

(Hart, JBMR, 2007)
Onset of manifestations of affected tissues

- **Fibrous dysplasia**
- **Café-au-lait**
- **Precocious Pub.**
- **Thyroid**
- **Phosphate**
- **Growth hormone**
- **Cushing’s**

- **sub/pre-clinical**
- **clinically evident**
- **spontaneous resolution possible**

Complete staging after age 5+ allows for determination of most affected and unaffected tissues.
What are the effects of endocrine dysfunction on FD?

Untreated endocrine dysfunction makes FD worse

(Leet, JBMR, 2004)
The causes of FD/MAS are targets for treatment

**Better surgical devices and techniques:**
better devices for children, comparison of techniques

**“stem cell” therapy:** replace mutant cells with normal cells

**Cell to cell and intracellular communication:** identify and block the communication system in affected cells

**Small molecule drugs:** molecules that act specifically at the mutant protein

**Oligonucleotide therapy:** small stretches of DNA/RNA that block the mutant gene

**Gene therapy:** replace the mutant gene with a normal gene
Targets for treatment & care to promote improved quality of life

- gene
- protein
- cells
- tissue
- FDA
- pharma
- researchers
- physicians/therapists
- support groups
- patients/families
- trials
Targets for treatment & care to promote improved quality of life
What FD Does

What amazing people with FD Do!
One day FD won’t do this!

People with FD will be even more amazing!
Thank you: to the patients, families, and co-workers

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