Precision Medicine in Pediatric Oncology

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Advances in outcome for patients with pediatric cancers have come at a price

Cancer is the leading cause of disease-related death in children

2/3 of survivors have long-term side effects

Identifying cancer causing mutations

Mutations result in activation of oncogenes or loss of tumor suppressors

Cancer cell

The Encyclopedia Britannica has 300 million letters
The amount of information in a cell = 10 x Encyclopedia Britannicas

Normal cell

Sequencing all 25,000 genes in the human genome

2009: Steve Jobs was the 20th person to have his genome sequenced
• 4 institutions (Stanford, JHU, Harvard, Broad)
• 4 months
• $100,000

Actionable alterations: Directing patients to targeted therapies

5 yr relapse with AML
Nkx3.1(AML1-ETO) AM51-410
4 cycles of standard AM therapy

Relapse

Salvage chemo

BMT bone marrow transplant

Day +100

Maria Luisa Sulis

Leukemia

Normal

cKIT Asn655Lys
### Actionable alterations: Directing patients to targeted therapies

**Graph:**
- **cKIT Asn655Lys**
- **Leukemia** vs. **Normal**

**Axes:**
- **X-axis:** Days on Imatinib
- **Y-axis:** Leukemia blasts (%)

#### 8 years
- **Chemos:**
  - paclitaxel/carboplatin
  - gemcitabine/docetaxel
  - paclitaxel/hormonotherapy
  - rapamycin
- **IP-Chemo**
- **Local control:**
- **Bone marrow transplantation**
- **Sanger sequencing**
- **Human genome**
- **Local gene sequencing**

#### Precision medicine, personalized care

**Graph:**
- **ETV6-NTRK3 fusion**
- **LOXO-101**

**Single patient use, 1 month**

### Strategic vision for Pediatrics

- **Create an expansive ecosystem that expands our reach and impact for children with cancer:**
  - Strengthen the “Core”
  - Restructure to leverage a unique care platform
  - Recruit national stature service chiefs
  - Recruit leadership and build a world class translational research program
  - Develop a pioneering genomics/genetics program
  - Address barriers to drug access
  - Expand access and reach
    - 7-day/week clinic
    - Expand into Regional sites
    - Establish strategic partnerships with other centers

### What next?

- **8 years**
- **Ipatasertib**
- **Compassionate use, 1 month**

### 2017 MSK Society Prize

Nomination Committee:
- Andrew Kung
- Richard O'Reilly
- Scott Armstrong (DFCI)
- Charlie Roberts (St. Jude)
- Mignon Loh (UCSF)

Dr. Jim Downing
President and CEO, St. Jude
MSKCC, Board of Scientific Consultants
HOPP, External Advisory Board