Patient-Driven Treatment of Hand Contractures in Epidermolysis Bullosa

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To
For


To
Hands
For


To
Hands
For
Patients

Patients who have had hand surgery:

- “It took forever to heal the hand”
- “The skin graft donor sites never healed”
- “The contractures came back in a few months”
- “It didn’t help my function at all”
- “It was so painful”
- “I’m never having hand surgery again!”

Patients who want hand surgery:

- “I was doing fine until I lost my thumb.
- “I want my independence back.”
- “Is there anything you can do for me?”

Two Questions for Patients/Parents

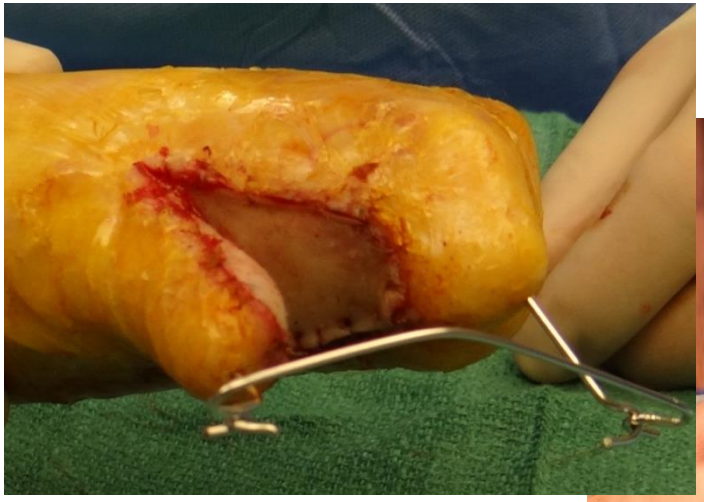
- What can I do FOR you?
  - Help patients achieve their goals
- What do you not want me to do TO you?
  - Minimize the cost of our treatments

Surgical Strategy

- Increase the distance between the thumb and the hand
  - First webspace inlet width

Surgical Strategy

- Use skin graft to prevent long healing time, need for dressing changes
  - Elbow donor site



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  - Need validated patient-reported outcome measures
  - Nothing reported in the literature

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Hand Function and Quality of Life in Children with Epidermolysis Bullosa

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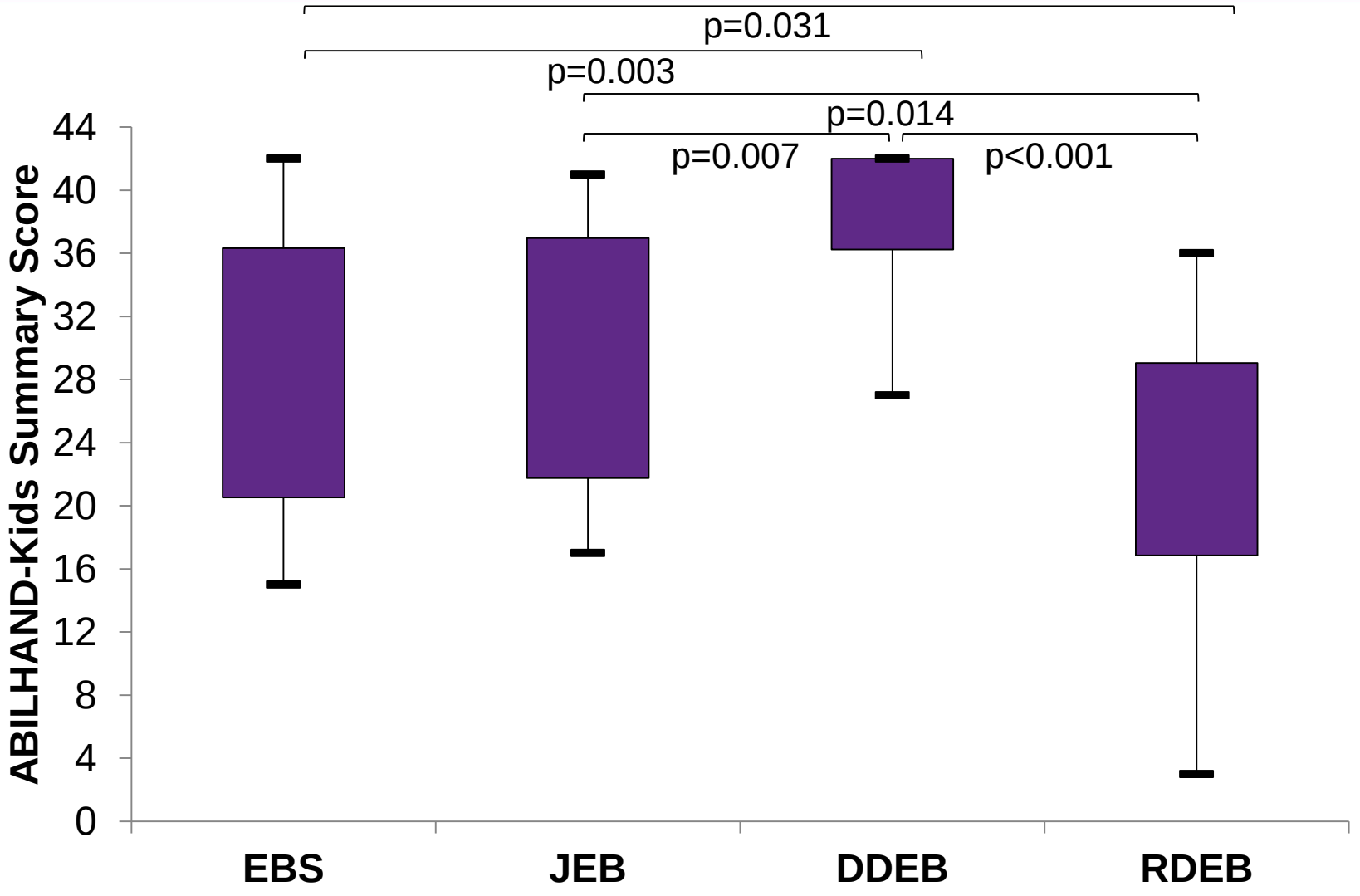
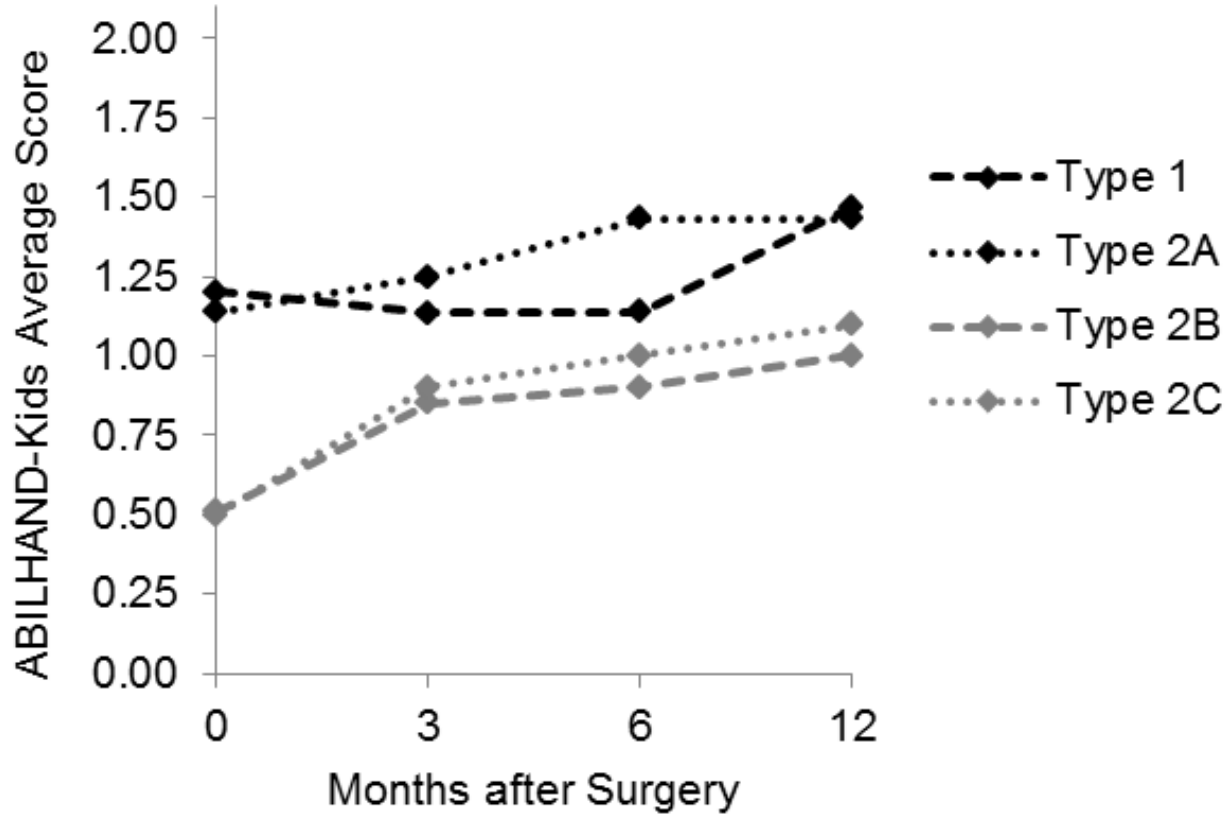
ABILHAND-Kids



Thumb Release

Effects of Hand Surgery

- Hand Function (ABILHANDS)



B

*Higher values indicate better function

An Example

Left Hand

Right Hand

Release with FTSG from elbow

But…

- Donor site never fully healed

Left Hand – What to do?

No Skin Graft

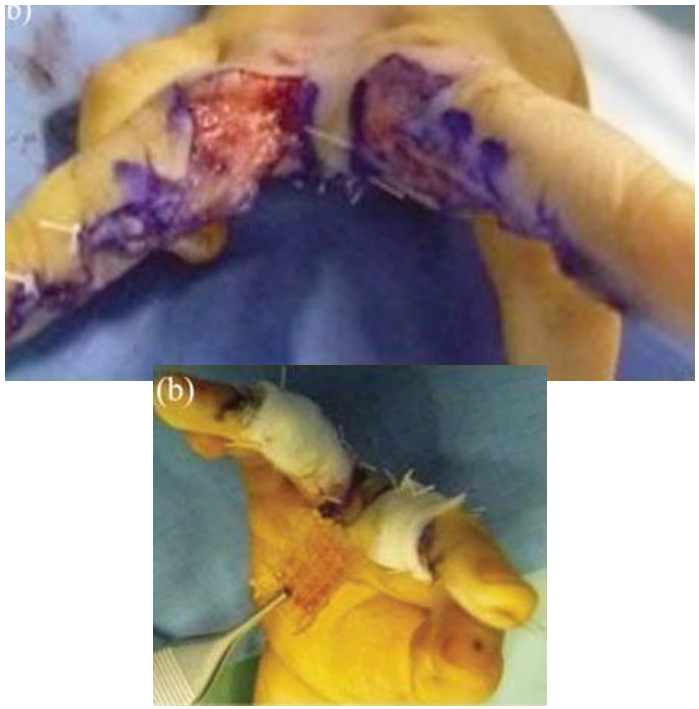
- Amy Ladd, MD
  - Stanford University

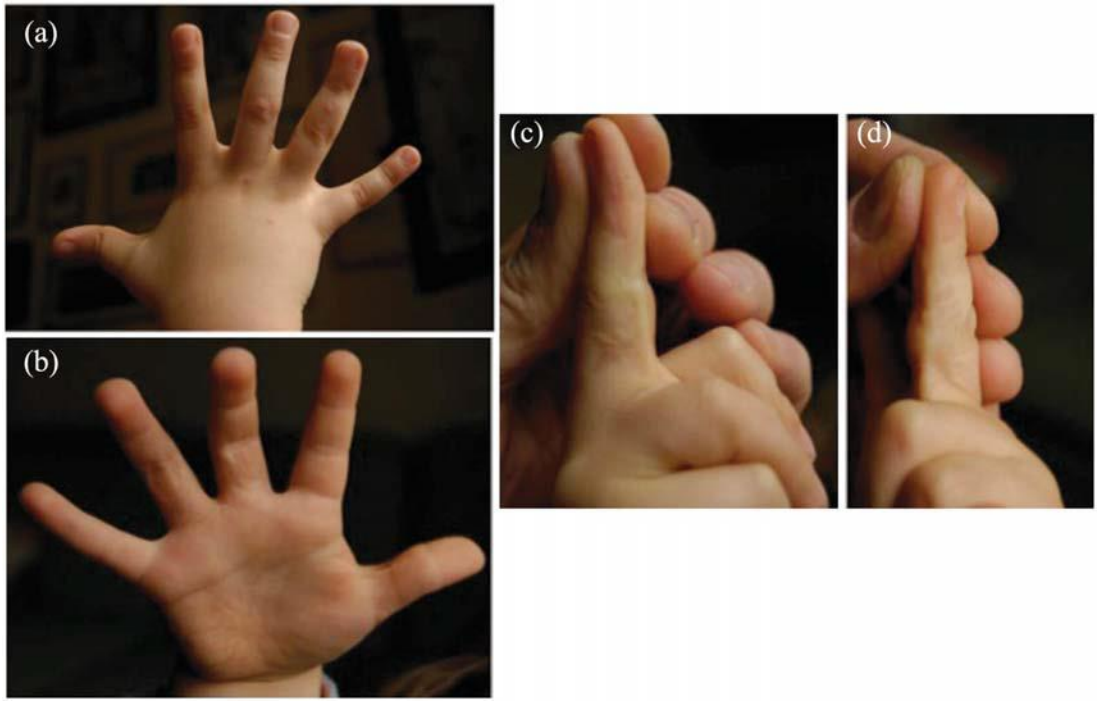
Surgical Treatment and Postoperative Splinting of Recessive Dystrophic Epidermolysis Bullosa

Amy L. Ladd, MD, Alice Kibele, OTR, Sheila Gibbons, LVN,
Stanford, CA

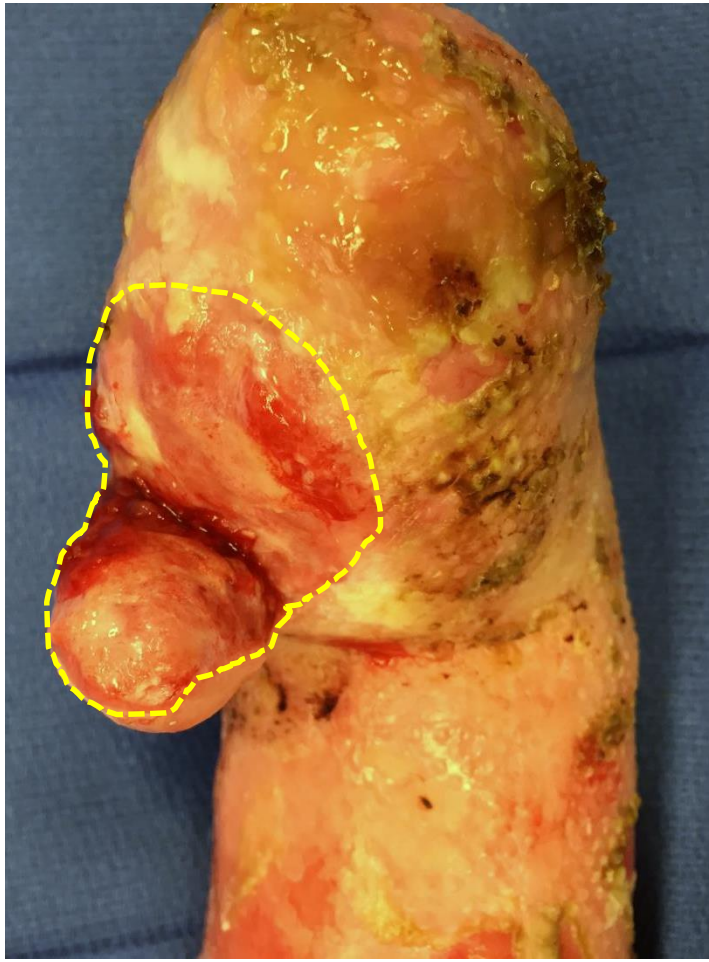
Skin Graft Substitute

- Landi et al, JHS(E) 2014
  - Hyaluronic acid matrix
  - 22 congenital syndactyly patients, 2 year f/u





Hyalomatrix



Another Child

Another Child

Similar to skin graft result

- 20 FTSG, 20 Hyalomatrix…

Wound healing (good)

Wound healing (not good)

Wound healing (not good – FTSG)

Maybe it's not the surgery…

- What drives the contracture phenotype?
- What drives wound healing?

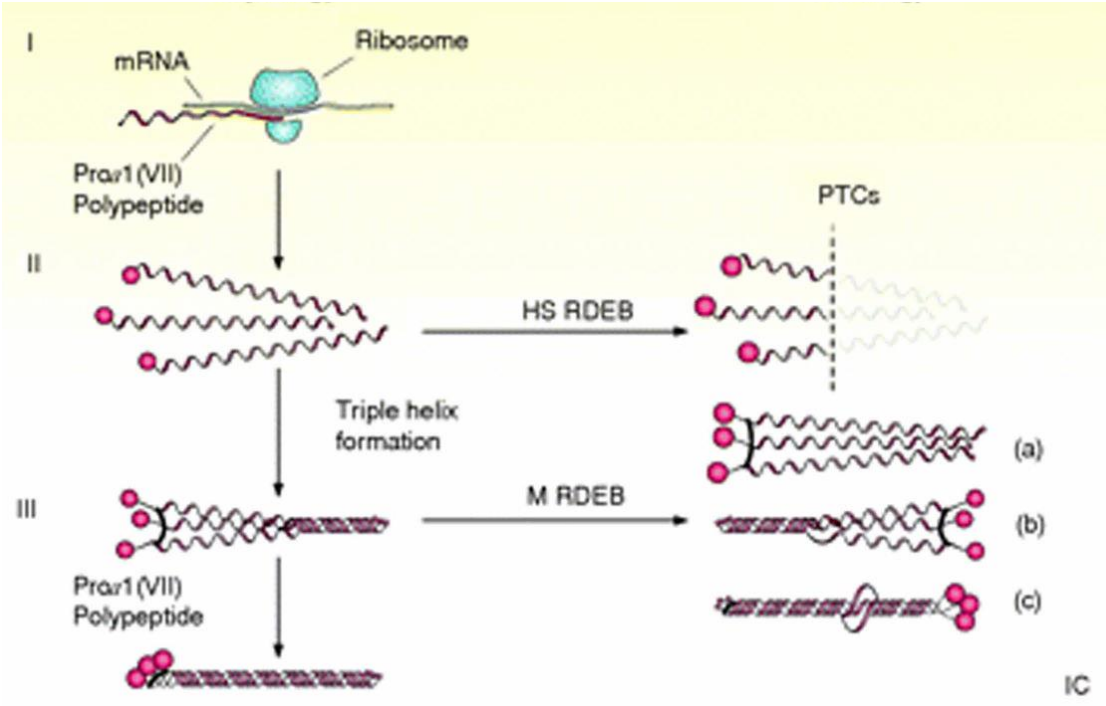
Genotype-Phenotype Correlation

- Does *COL7A1* genotype drive hand contracture phenotype?

DebRA Chile

Genotype-Phenotype Correlation

- 38 RDEB patients
- Genotype
  - NP: no protein
  - AP: abnormal protein



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- Phenotype
  - Pseudosyndactyly
  - Cocoon hand

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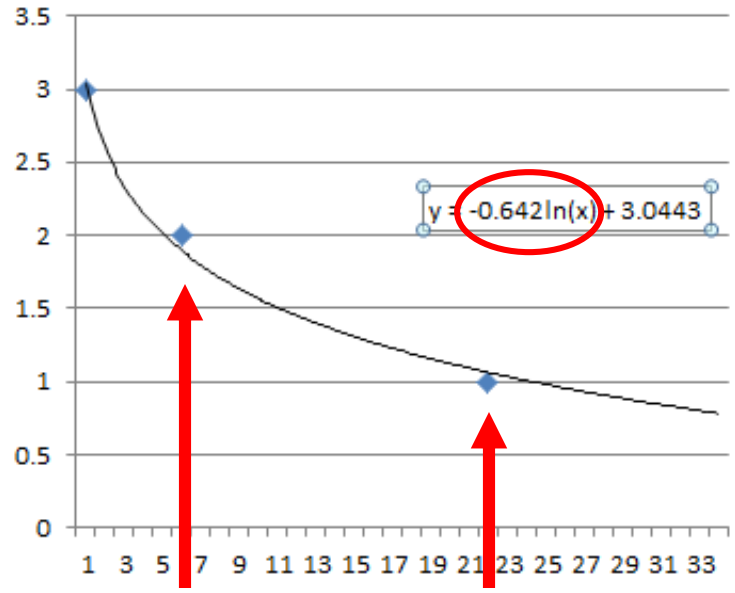

Genotype-Phenotype Correlation

- AP genotypes have less severe phenotypes
  - p<0.001, Mann-Whitney

Joint consequence (2 mutated alleles)	Hand Phenotype log_score
2/2 Shorter protein	0
1/2 Shorter protein	0
1/2 1 aa different protein	0
1/2 Shorter protein	0
1/2 Shorter protein	0
NO protein	0
NO protein	0
NO protein	0
1/2 Shorter and 1/2 1 aa different protein	0.285
1/2 Shorter protein	0.316
NO protein	0.334
1/2 Shorter protein	0.338
NO protein	0.342
NO protein	0.344
NO protein	0.361
1/2 Shorter protein	0.363
NO protein	0.366
NO protein	0.371
NO protein	0.379
NO protein	0.394
NO protein	0.395
NO protein	0.4
NO protein	0.403
NO protein	0.449
NO protein	0.467
NO protein	0.489
NO protein	0.509
NO protein	0.6
NO protein	0.612
NO protein	0.642
NO protein	0.645
NO protein	0.66
NO protein	0.694
1/2 1 aa different protein	0.702
NO protein	0.721
NO protein	0.819
NO protein	0.874
NO protein	0.89
NO protein	1.19
1/2 Shorter protein	1.443
NO protein	1.82

Genotype-Phenotype Correlation

- AP genotypes have less severe phenotypes
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  - One 75yo with normal hands (homozygous AP)

Joint consequence (2 mutated alleles)	Hand Phenotype log_score
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Genotype-Phenotype Correlation

- AP genotypes have less severe phenotypes
  - p<0.001, Mann-Whitney
  - One 75yo with normal hands (homozygous AP)
- Two AP genotypes had severe phenotype
  - One accelerates degradation
  - One severely reduces expression

Joint consequence (2 mutated alleles)	Hand Phenotype log_score
2/2 Shorter protein	0
1/2 Shorter protein	0
1/2 1 aa different protein	0
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Genotype-Phenotype Correlation

Genotype-Phenotype Correlation

- Genotype does not correlate with patient-reported hand function

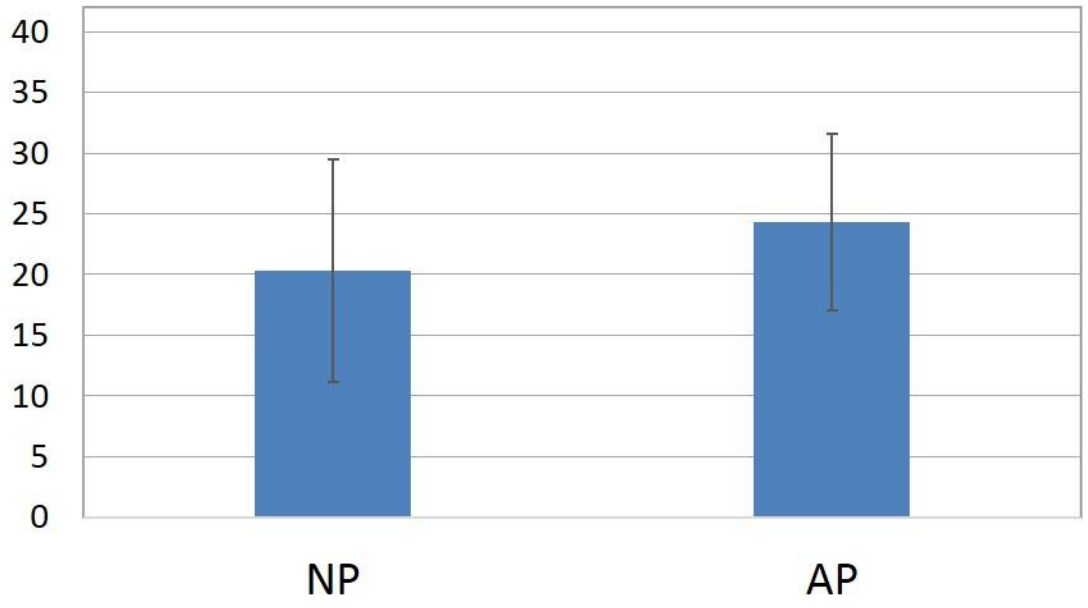

Figure 5: Mean ABILHAND-Kids score (higher score indicates better hand function, out of a maximum 42 points) between genotypes that confer no collagen VII protein expression versus those that confer at least some abnormal protein expression.

Moving Forward

- Need better hand function assessments/measurements
  - Determine treatments required
  - Compare therapeutic strategies
- Need better understanding of contractures
  - Pathogenesis
  - Prevention
- Need better biological therapies
  - EB is not a surgical disease
- Need to work together…

Moving Forward

Consensus

1.
2.
3.
4.

Consensus

1. Prevention is better than surgery.
2.
3.
4.

Consensus

1. Prevention is better than surgery.
2. Wound coverage strategy doesn’t matter.
3.
4.

Consensus

1. Prevention is better than surgery.
2. Wound coverage strategy doesn’t matter.
3. The thumb is the highest priority.
4.

Consensus

1. Prevention is better than surgery.
2. Wound coverage strategy doesn’t matter.
3. The thumb is the highest priority.
4. Patient needs should drive decisions.

Song: “Stille Nacht” comp. Franz Xaver Gruger, 1818, Obendorf bei Salzburg


Thank
You