REPRODUTIVE STRATEGIES
AND WRAP-UP

Chip Wilmot, MD, PhD
DISCLAIMER

- The information provided by speakers in any presentation made as part of the 2017 NAF Annual Ataxia Conference is for informational use only.

- The NAF encourages all attendees to consult with their primary care provider, neurologist, or other health care provider about any advice, exercise, therapies, medication, treatment, nutritional supplement, or regimen that may have been mentioned as part of any presentation.

- Products or services mentioned during these presentations does not imply endorsement by the NAF.
PRESENTER DISCLOSURES

- No relationships to disclose or list
PRESENTER DISCLOSURES

- No relationships to disclose or list
- Sex will be mentioned
STRATEGIES TO DEFEAT ATAXIA

- Live Well, Fight Hard … aka the “Kyle Bryant Method”

- www.kyleabryant.com
STRATEGIES TO DEFEAT ATAXIA

• Live Well, Fight Hard … aka the “Kyle Bryant Method”
• Develop Treatments
STRATEGIES TO DEFEAT ATAXIA

• **Live Well, Fight Hard** … aka the “Kyle Bryant Method”

• **Develop Treatments**
  - Understand Disease Mechanism
  - Develop rational therapeutic strategies
    - “preclinical” lab science
  - Develop testing methods
    - Establish measures of disease, trial network
  - Conduct trials
    - Mostly with companies
  - Provide treatment
    - FDA approval
    - Insurance coverage
STRATEGIES TO DEFEAT ATAXIA

• Live Well, Fight Hard  ... aka the “Kyle Bryant Method”
• Develop Treatments
  • Helpful for an affected individual
• Banish the Disease
  • Helpful for others
STRATEGIES TO DEFEAT ATAXIA

• Live Well, Fight Hard … aka the “Kyle Bryant Method”

• Develop Treatments
  • Helpful for an affected individual

• Banish the Disease
  • Helpful for others
  • Only works for genetic ataxias
  • No Mutated Gene ===> No Disease
  • Most helpful for Dominantly inherited ataxias
STRATEGIES TO DEFEAT ATAXIA

• Banish the Disease
STRATEGIES TO DEFEAT ATAXIA

• Banish the Mutant Gene
STRATEGIES TO DEFEAT ATAXIA

• Banish the Mutant Gene
  • Don’t ever have sex -- abstinence
STRATEGIES TO DEFEAT ATAXIA

• Banish the Mutant Gene
  • Don’t ever have sex -- abstinence
  • Have “protected” sex -- birth control
STRATEGIES TO DEFEAT ATAXIA

• Banish the Mutant Gene
  • Don’t ever have sex -- abstinence
  • Have “protected” sex -- birth control
  • What if you want to have children?
STRATEGIES TO DEFEAT ATAXIA

• How to have a child
STRATEGIES TO DEFEAT ATAXIA

• How to have a child without passing on the bad gene
STRATEGIES TO DEFEAT ATAXIA

• How to have a child without passing on the bad gene
  • Borrow your neighbors child
STRATEGIES TO DEFEAT ATAXIA

• How to have a child without passing on the bad gene
  • Borrow your neighbors child
  • Get a spouse who already has kids (the stepkid solution)
STRATEGIES TO DEFEAT ATAXIA

• How to have a child without passing on the bad gene
  • Adopt
  • Unaffected Sperm Donor (for affected males)
  • Unaffected Egg Donor (for affected females)
    • In vitro fertilization (you become pregnant)
    • Surrogate pregnancy (another woman becomes pregnant)
IN VITRO FERTILIZATION

1. Stimulation of ovaries
2. Egg retrieval from ovaries
3. Fertilisation of eggs
4. Embryo maturation
5. Transfer of embryo to uterus

The IVF cycle
STRATEGIES TO DEFEAT ATAXIA

• How to have a child without passing on the bad gene (that is 100% genetically related)
  • Test after usual pregnancy has started
    • Amniocentesis, chorionic villous sampling
    • Terminate the pregnancy if the fetus has the disease
  • Test before unusual pregnancy has started
    • Preimplantation Genetic Diagnosis (PGD)
STRATEGIES TO DEFEAT ATAXIA

• **Preimplantation Genetic Diagnosis (PGD)**
  • Allows the selection of unaffected embryos
  • Children are 100% genetically related to parents

• IVF ➔ test young embryos for the mutation ➔ implant unaffected embryos
Strategies to Defeat Ataxia

- Pre-implantation Genetic Diagnosis (PGD)
STRATEGIES TO DEFEAT ATAXIA

• **Pre-implantation Genetic Diagnosis (PGD)**
  • Considerations:
    • Ethical/moral/religious
    • Cost $10-15,000
    • Hassle
    • Efficiency ~50%
STRATEGIES TO DEFEAT ATAXIA

• Pre-implantation Genetic Diagnosis (PGD)
  • CAN be done in at-risk parents who don’t want testing
  • If you are interested:
    • Talk to your physician
    • See a genetic counselor or geneticist
    • Find a fertility clinic
WRAP-UP

• Camille Daglio and Joel Sutherland
  • NAF is 60!!!
  • NAF 6 consecutive 4-star ratings by Charity Navigator
  • “Money buys research, … “
WRAP-UP

• Camille Daglio and Joel Sutherland
  • NAF is 60!!!
  • NAF 6 consecutive 4-star ratings by Charity Navigator
  • “Money buys research, Research buys answers“
  • “Think big, but its still one step at a time”
  • “The only thing you can’t do is nothing”
  • 60 for 60
  • NAF new look
WRAP-UP

• Pravin Khemani
  • Types of ataxia
  • Multidisciplinary care
  • Team approach
  • Seek out experienced neurologist
• Jason Wolfer
  - Glimpse of what it means to have ataxia
  - “Everyone has a number. I wanted one too.”
  - SCA 24-7
  - Experiences with neurologists
    - (Note to self – don’t underestimate patients!!)
  - Importance of meeting people and support
  - "The hammer that shatters the glass is the same hammer that shapes the metal"
  - Denial, Isolation, Acceptance, Support
  - “My life had been invaded by a very stubborn guy sho wasn’t going away soon”
• Huda Zoghbi
  • SCA1 mouse models
    • polyQ expansion makes it more stable
    • S776 phosphorylation is needed for toxicity
    • Strategy: lowering ataxin-1 levels
      • Antisense Oligonucleotides (ASO)
        • help mice, esp. lifespan
        • Works in humans in other diseases (Spinal Muscular Atrophy)
        • Need to prove target engagement
        • Need to dose properly to make it safe (might affect other genes like Capicua)
    • Find genes that lower ATXN1 levels (MSK1 … which phosphorylates S776)
• Henry Paulson
  • Clinical Trial Readiness
  • Finding genes
    • “Can’t find answers unless you toil in the lab”
• Common Mechanisms
  • DNA repair
  • Channel dysfunction
  • Bioenergetics
  • polyQ toxicity
  • Protein homeostasis
  • Repeat expansions
WRAP-UP

• Brent Vogel
  • Genes! Genes! SCA43, SCAR24
  • Types of testing -
    • Single genes, gene panels. Whole Exome Sequencing
  • Identifying new genes
  • 9 yo girl found to have a treatable condition (high dose riboflavin)
  • Benefits of testing
    • Stop unnecessary treatment
    • Get an answer
    • Prognosis
    • Treatment (of course)
• Terri Alessi
  • Caregiver for husband and son with SCA2
  • You have to proactive in letting your needs known, accept help
  • Financial impact
  • Love for her family and such poise!
  • “Walk for Dave”
• Laura Ranum
  • NAF research grants
  • Many applications (102 covering many diseases), many reviewers, conference calls etc.
  • $1.1 million for 27 projects (26%)
  • Pioneer SCA Translation Research awards described in more detail
  • Gene discovery → Gene based therapies
    • Mutation types
    • Genetics 2017 - RAN translation
    • Gene Editing and targeting possibilities
• THANK YOU!!!
  • Patients
  • NAF
  • FARA
  • nurse coordinators - Becky McMurray, Cathy Wood-Siverio, Betty Robinson, Sue Gronka
  • Industry partners – Reata, Biohaven, Shire, Santhera