

REPRODUCTIVE STRATEGIES AND WRAP-UP

Chip Wilmot, MD, PhD



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PRESENTER DISCLOSURES

- No relationships to disclose or list

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- Sex will be mentioned



STRATEGIES TO DEFEAT ATAXIA

- **Live Well, Fight Hard ... aka the “Kyle Bryant Method”**
- www.kyleabryant.com





STRATEGIES TO DEFEAT ATAXIA

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- **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

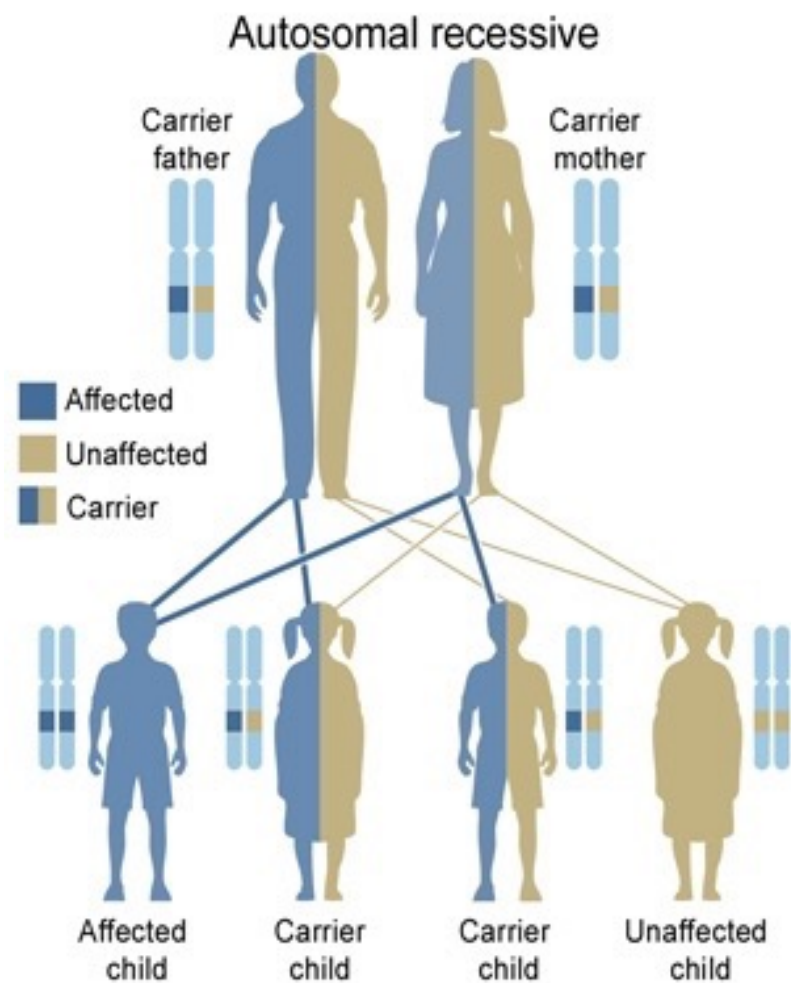


STRATEGIES TO DEFEAT ATAXIA

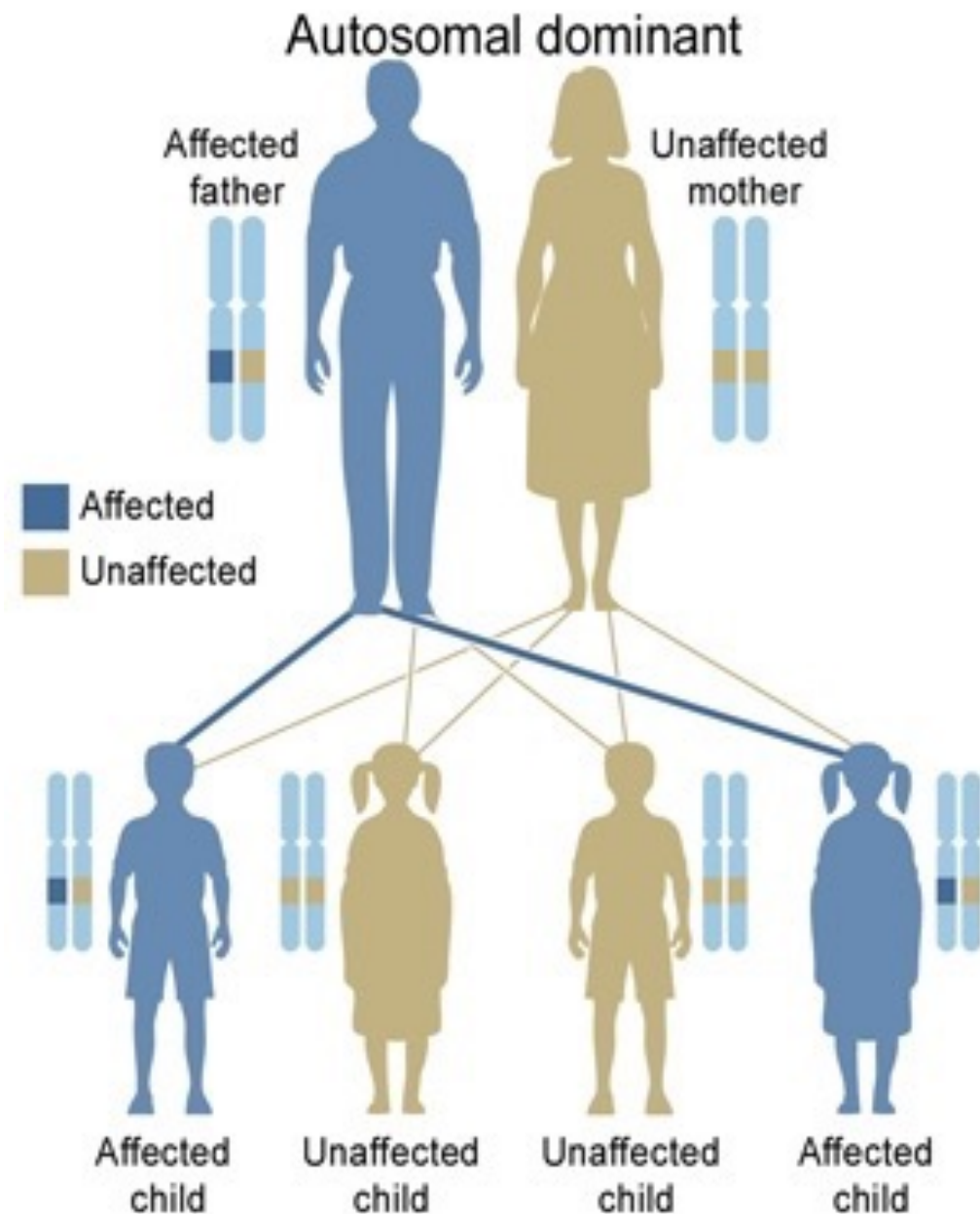
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- **Develop Treatments**
 - Helpful for an affected individual
- **Banish the Disease**
 - Helpful for others

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



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STRATEGIES TO DEFEAT ATAXIA

- **Banish the Disease**



STRATEGIES TO DEFEAT ATAXIA

- **Banish the Mutant Gene**



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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

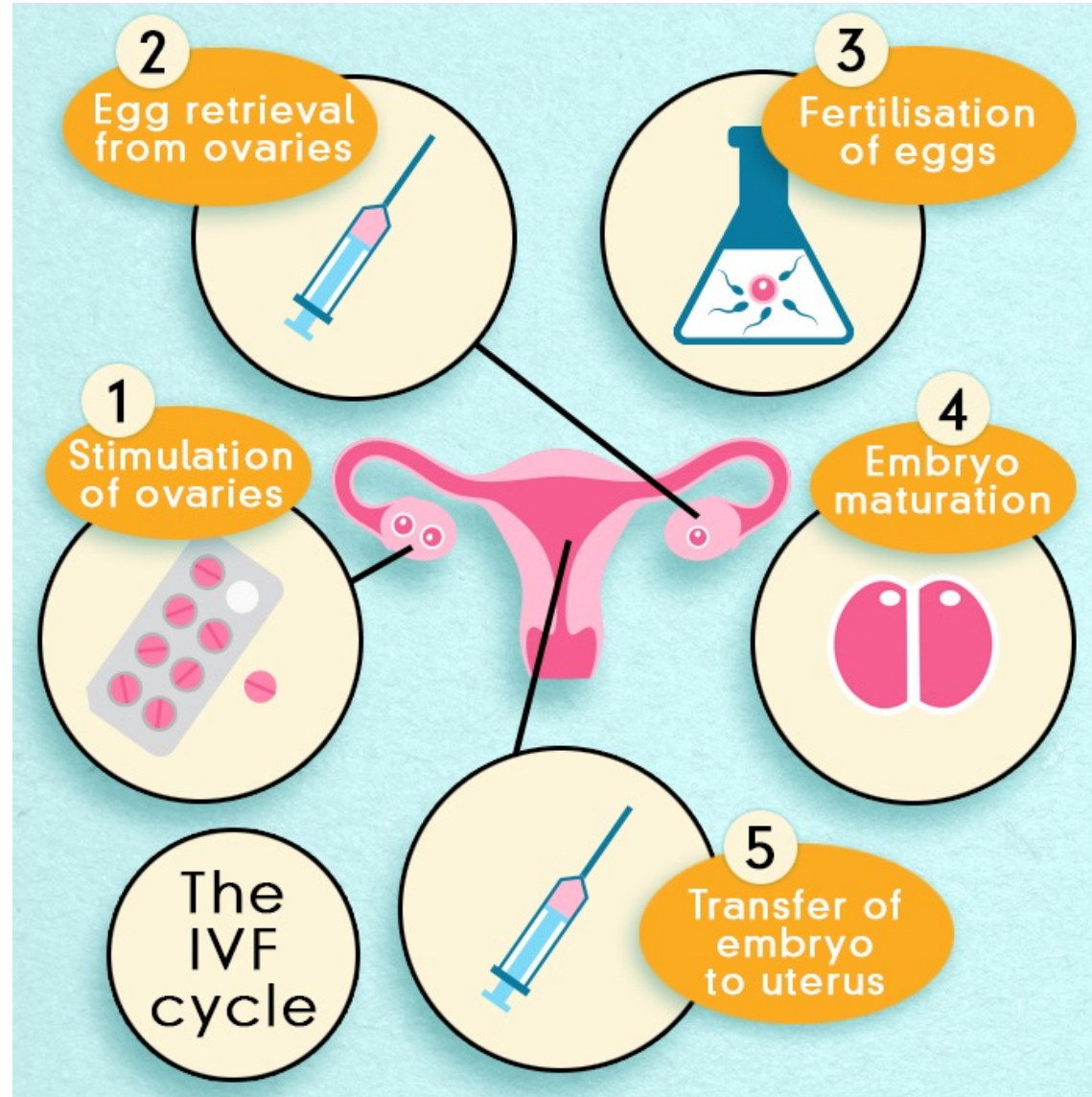
STRATEGIES TO DEFEAT ATAXIA

- **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



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)

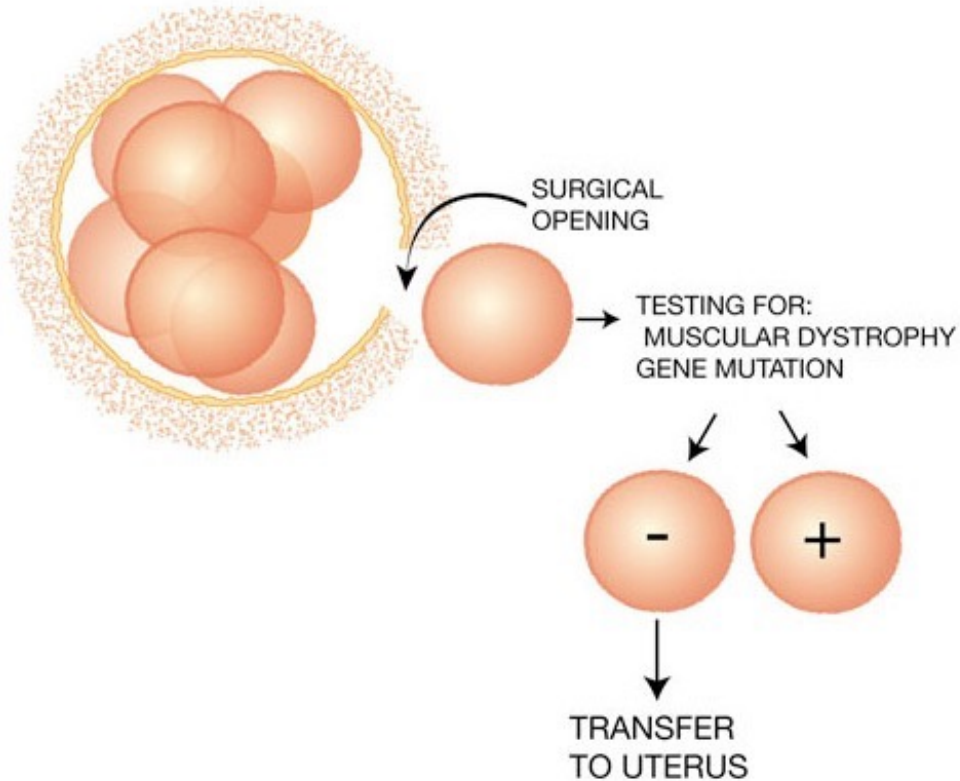
STRATEGIES TO DEFEAT ATAXIA

- **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)**

DAY-3
8-CELL EMBRYO



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

WRAP-UP

- 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 who wasn’t going away soon”

WRAP-UP

- 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)

WRAP-UP

- Henry Paulson
 - Clinical Trial Readiness
 - Finding genes
 - “ Can’t find answers unless you toil in the lab”
 - Common Mechanisms
 - DNA repair
 - Chennel 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)



WRAP-UP

- 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”

WRAP-UP

- 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