Epilepsy & Movement Disorders

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About Michael Kruer

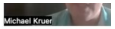
Dr. Michael Kruer is the Program Director for Pediatric Movement Disorders at the Barrow Neurological Institute Phoenix Children's Hospital

Publications:

Bi-allelic variants in SPATA5L1 lead to intellectual disability, spastic-dystonic cerebral palsy, epilepsy, and hearing loss

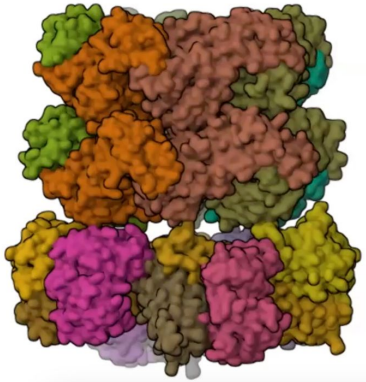
About Michael Kruer

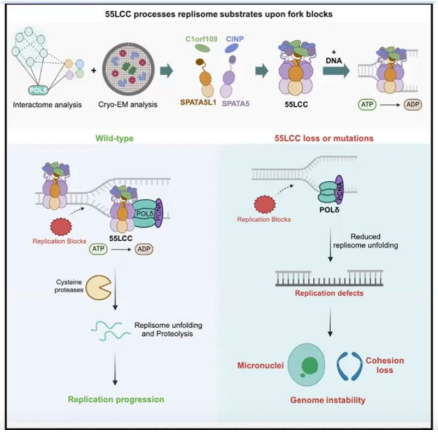
SPATA5 and SPATA5L1 together with AIRIM and CINP create one big protein complex



The SPATA disorders (aka 55LCC complex conditions)

- 55LCC (60s Large subunit Clearance & Chromatin complex)





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Epilepsy

What is Epilepsy?

- Repeated seizures
- The brain works by using electrical signals to communicate
- Seizures are caused by a ‘power surge’ in the brain
- Children with SPATA disorders are at a high risk for seizures

During a Seizure

- The brain’s normal rhythms are overactive (causes things to happen that shouldn’t) or disrupted (causes interruption of normal function)
- If rhythms are overactive, a child may stiffen, jerk, or make a sound
- If rhythms are interrupted, ‘freezing’, staring, or drooling may occur
- Most seizures are short and stop on their own, but each person’s seizures tend to have their own patterns

Epilepsy

Why seizures occur

- Brain cells send unbalanced electrical signals
- Seizures can be triggered by fever, illness, missed medication, or lack of sleep
- We know that seizures are common in children with SPATA disorders

Different types of seizures

- Focal Seizures: Affect one area
  - Child may be aware or unaware
- Generalized Seizures: Affect both sides of the brain at once
- Absence Seizures: Brief staring spells
  - Important to recognize that not every state is a seizure

Epilepsy in SPATA Disorders

- Frequency
  - 40-70% of those with SPATA disorders have epilepsy
- Age of Onset
  - Typically infancy or early childhood
- Seizure Types
  - Generalized tonic-clonic, myoclonic, focal, epileptic spasms, infantile spasms, tonic
  - Some cases of Infantile Epileptic Encephalopathy
  - Some cases of Lennox-Gastaut
- EEG/MRI Findings
  - EEG: multifocal discharges, hypsarrhythmia-like in early onset cases, burst-suppression or multifocal spikes
  - MRI: hypomyelination, thin corpus callosum, cerebellar atrophy, PVL-like white matter loss
- Notes
  - Often drug-resistant, seizures may lessen with age
  - Epilepsy co-occurs with spastic-dystonic CP-like motor phenotypes
  - Many meet criteria for “Development and Epileptic Encephalopathy”

Diagnosing Epilepsy

- Doctors will ask about your child's birth, development, and medical history
- Additional questions about seizure features, patterns and changes over time will likely be asked as well
- An EEG will typically be performed to record brain waves during rest and sleep
- An MRI will usually be done to look for changes in brain structure
- Epilepsy is a clinical diagnosis with many factors at play

During a Seizure

- Stay calm to protect your child from injury
- Get your child to a flat surface and turn them on their side to keep their airway clear
- Time the seizure and note what happens. Be prepared to give rescue medication or call 911 if needed
- Most seizures will stop on their own after a few minutes
- Many seizures will trigger a stress response, causing blood to be moved from the skin to vital organs like the heart and brain. It’s rare for a child to need additional oxygen.

During a Seizure

Rescue Medication

- Children with epilepsy should have a seizure action plan
- Even if you never need it, you will feel better knowing you have it
- This includes a rescue medication such as intranasal midazolam or diazepam, rectal diazepam, or clonazepam wafers, as well as clear instructions about when to give it

What to Call EMS

- When concerned - the emergency medical system is there for you
- When you have given the rescue medication and the seizures continues (this is not common), usually the 5 minute mark
- Breathing or color is not returning to normal
- If injury has occurred or repeated seizures close together are happening

Preventative anti-seizure medication

- The mainstay of epilepsy treatment is prevention of seizures with a daily medicine
- Doses are based on weight and age
- It is important to take medication as prescribed and on schedule in order for it to be effective
- Sometimes, medications can cause side effects, and we don’t want treatment to be worse than the condition itself
    - Kids will often “settle in” to a medication despite early side effects
    - Talk to your doctor if you have concerns about lasting side effects

Treatment

Treatment Goals

- No seizures (or as few as possible)
- No side effects (or the closest we can get)
- We want to minimize seizure-related disruptions or injuries

Monitoring

- Common side effects can include tiredness and changes in mood or appetite
- Bring up any concerns to your child's neurologist
- Many anti-seizure medications are monitored with blood tests, but side effects may be idiosyncratic

Treatment

Other Treatments - Diet

- The ketogenic diet or Modified Atkins Diet may be effective for some children with seizures
  - Data is limited for children with SPATA disorders

Other Treatments - Epilepsy Surgery

- Epilepsy surgery, rather than being a treatment of last resort, can be highly effective for the right candidates
  - Surgery can greatly improve seizure control and sometimes even development
- Typically considered after 2+ medications have failed to control seizures
- Works by removing or disconnecting the source of the seizures
  - Most of the time, focuses on a specific part of the brain that is misbehaving
- However, most SPATA5 and SPATA5L1 patients have widespread abnormalities on brain MRI rather than focal ones

Treatment

Other Treatments - Neuromodulation (devices)

- VNS (Vagus Nerve Stimulator): Sends small pulses from the Vagus Nerve up to the brain to reduce seizures
- RNS (Responsive Neurostimulator): Zaps developing seizures as they start to occur
- DBS (Deep Brain Stimulator): Provides regular pulses within the brain to keep seizures from organizing
- These treatments can be valuable approaches; best decided on at an epilepsy center that offers all options

Outside the Home

- Family members, teachers, and therapists should be familiar with seizure features and first aid (recovery position, rescue medication)
- Always asks “what if…” and watch and support your child around water and with a helmet when appropriate
- Encourage independence but provide safety

SPATA-specific Recommendations

- We don’t have enough data to know if certain medications are more effective for people with SPATA disorders
- We do know that epilepsy in SPATA disorders is often mixed and difficult to treat
    - There is not likely to be a single one-size-fits-all approach to seizure treatment
    - Instead, a multidisciplinary approach tailored to your child’s needs is likely to be best
- This will ideally balance medications that can be effective for your child’s seizure types with any side effects your child experiences

Looking Ahead

- The SPATA registry can collect data about seizure treatments and seizure outcomes
    - The ability to do this will depend on the quality of the data within the registry
- Attracting new researchers to the field is important to help identify the most effective current treatments and to help develop new ones

Pediatric Movement Disorders

- SPATA disorders are not known to cause weakness due to a disease of the muscle or nerves themselves
- Most physical disabilities in patients with SPATA disorders appear to be due to movement disorders driven by brain dysfunction
- Similar to seizures, movement disorders arise when brain electrical activity is imbalanced, disrupting the regulation of movement

Brain Control of Movement

- The brain sends signals down the spinal cord, to the nerves, and out to the muscles, turning them on/off like a conductor directing an orchestra
- If the conductor's timing is off, the orchestra may activate the wrong muscles, at the wrong time, or in the wrong ways
- This can lead to unwanted, involuntary muscle activations or to difficulty getting a person's body to do what they want it to do (and when they want to do it)

How does this show up?

- In infants, these issues can show up as feeding problems, gassiness/fussiness/vomiting, and missed milestones
- Over time, muscle tightness, excessive movements, and inability to support one's body are common
- This commonly leads to developmental delays or physical disabilities. Many children with SPATA disorders may be diagnosed with cerebral palsy

Cerebral Palsy

Cerebral Palsy (CP) is a neurodevelopmental disorder that affects motor function

Making a SPATA5 or SPATA5L1 diagnosis does not “undiagnose” epilepsy or CP; instead, there can be value in dual diagnosis

- Most people in schools or communities will be families with epilepsy or CP as developmental diagnoses but not SPATA disorders, so this can be the start of a dialogue

<u>Types of CP (broken down by movement disorder)</u>

- Hypotonia: muscle floppiness; often accompanied by difficulty in activating the muscles (weakness)
- Spasticity: consistent muscle tightness
- Dystonia: fluctuating muscle tightness and posturing
- Chorea: jumpy, jerky movements that often migrate from body part to body part

Making a Diagnosis

- MRI may be helpful to understand how any changes in the structure of the brain, but movement disorders can’t be detected on an EEG
- A trained specialist can recognize different movement disorders and examine the person with a SPATA disorder to diagnose a movement disorder
    - Videos can be very helpful, especially if your child naps or the movement disorder comes and goes
- The right diagnosis is key to developing the right treatment plan - different movement disorders are treated differently

How can movement disorders affect your child?

- By causing pain or distress
- By interfering with normal function
  - Movement disorders can make it hard for affected individuals to walk, talk, speak, and use their hands
  - Movement disorders can impede progress in therapy
- By disrupting normal growth and development of bones, muscles and joints
  - This can lead to orthopedic complications, such as hip dysplasia and scoliosis, as well as deformities of the feet, ankles, and other parts of the body

How can therapy help?

- Development proceeds in an orderly fashion, with each step building upon the prior one
- Physical, occupational, and speech therapy can help build core skills and identify workarounds for challenges
- Bracing and equipment can also be an important part of supporting your child

Medical Intervention

- To take away the bad stuff while leaving the good stuff
- Although movement disorders are challenging to treat, we want to remove your child's barriers as much as we can while allowing them to build their motor skills
- As a movement disorders specialist, I view my role as opening doors for kids - they still need therapy and hard work breakthroughs

Medical Intervention

Daily medication treatments

- Tailored to the movement disorder and your child's needs
- "Start low, go slow" and adjust to get the most bang for our buck
- Treatment plans need to be individualized

Other treatments - injection therapies

- Botulinum: shots can be given to "relax" overactive muscles, providing comfort and sometimes allowing function to improve
  - Can be given awake or asleep
  - Typically every 3-4 months
- Phenol: injections given into nerves
  - Typically done asleep
  - Usually given every 6 months

Medical Intervention

Other treatments - surgeries

- Selective Dorsal Rhizotomy
  - For Spasticity
- Intrathecal Baclofen Pump
  - For spasticity and/or dystonia
- Deep Brain Stimulation
  - For dystonia and/or chorea

Rescue Treatments

- Dystonia and chorea are prone to worsening in some people
- Dystonia or Chorea Action Plans should be offered to provide rescue medications
  - Commonly include steps (i.e. 1-3) and medications like diphenhydramine, clonidine, or diazepam

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When to activate EMS

- If the movement disorder is causing distress and not responding to rescue medication, families may need to call 911
- Hospitalization may be required for some patients

Considerations for SPATA Disorders

- Again data is limited
- Early hypotonia is often seen, with later spasticity and/or dystonia
- We have seen several patients with severe chorea
- Patient registry may allow data to be captured and analyzed and more conclusions to be drawn