

The IFCR Centers of Excellence: the Rett Clinic at Children's Hospital Colorado

Standards of Care

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The Rett Clinic Team:

**Scott Demarest MD; Margarita Saenz MD; Katie Angione MSGC;
Laura Watne MS RD, Margaret Spring MS OT, Meghan Roe M Ed,
CCC-SLP et al.**





Disclosures

1. RO1 NS076577 (Benke)

NIH/NINDS

Molecular mechanisms linking early life seizures, autism and intellectual disability

Role: PI.

2. Questcor Pharmaceuticals (Benke)

Whole-exome sequencing and ACTH responsiveness in Infantile Spasms

Role: PI.

3. 1U10NS077277(Vollmer)

NIH/NINDS

Rocky Mountain Network for Neuroscience Clinical Studies (NeuroNext Clinical Site)

Role: Co-I.

4. U54 HD061222 (Percy)

NICHD

Rett syndrome, MECP2 Duplication Disorder, and Rett-related Disorders Natural History.

Role: Site Director, Co-I.

5. Rett Clinic at Children's Hospital Colorado (Benke)

Rocky Mountain Rett Association

Role: PI/Medical Director

6. CDKL5 Center of Excellence (Benke)

International Foundation for CDKL5 Research

Role: PI

7. Neuren: Study of trofinetide, also known as NNZ-2566, for females with Rett Syndrome

Role: site PI



Topics today



- IFCR CDKL5 Centers of Excellence
- The Rett Clinic at Children's Hospital Colorado
 - Clinic profile
 - Research approach in a clinical setting

CDKL5 research consortium: IFCR Centers of Excellence



3 Teams

University of Colorado/Children's Hospital Colorado

Lead: Benke

Boston Children's/Harvard

Lead: Olson/Kaufmann

Cleveland Clinic

Lead: Parikh

Goals: Clinical Care tailored to CDKL5 syndrome, Advancing Research, determining Standards of Care





The Rett Clinic at Children's Hospital Colorado:

Established thanks to a generous and repeated gifts from the Rocky Mountain Rett Association (RMRA). Started December 14, 2011.

Purpose:

- Consultation and evaluation for all people with Rett Syndrome and genetically related disorders (MeCP2, CDKL5 and FOXP1)
- Ensure they are receiving the needed therapies, treatments and services to live a quality life.
- We serve people of all ages.
- Provide up-to-date information on Rett Syndrome, CDKL5 and FOXP1 to parents, physicians, therapists and care providers.
- Participate in ground-breaking clinical research trials.
- Work as a team with the family and the primary care providers.
- Train future providers
- Family support



What it looks like:

Integration through a multi-disciplinary approach to provide optimal care

RN coordinator driven (Tristen Dinkel RN BSN)

6x/year clinic

Providing new and follow-up assessments

Clinic appointment involves a four hour block with consultation by all pertinent specialists in one centralized location

The patient/family stays in one room with providers moving to the families' location in a robin format. Specialized Multi-D area.

4-5 new and 4-5 follow-up patients seen per session-

Intake packets filled out prior to visit (3 weeks)

- Team reviews over lunch 1 week prior to clinic
- Outside records reviewed and archived for completion
- Parent/therapist/provider questions
- Team addresses questions/concerns while in clinic.





Our Team:

18 members representing individual professional disciplines:

Timothy Benke, PhD, MD

Neurology/Medical Director

Tristen Dinkel, RN, BSN

Nurse Clinic Coordinator

Anne Stratton, MD

Rehabilitation

Sandra Friedman, MD, MPH

Developmental Pediatrics

Sumeet Garg, MD

Orthopedic Surgery

Terry Katz, PhD

Neurodevelopment & Behavioral Pediatrics

Margarita Saenz, MD

Clinical Genetics

Michael Schaffer, MD

Cardiology

Oren Kupfer, MD

Pulmonary

Jaime Guthrie, PT, DPT, CFMT

Physical Therapy

Margaret Spring, M.S., OT

Occupational Therapy

Meghan Roe M.Ed., CCC-SLP

Augmentative Communication Specialist

Laura Watne, MS RD

Nutrition

Ed Liu, MD

GI/Nutrition

Scott Demarest, MD

Neurology/Epilepsy

Katie Angione, MS, CGC

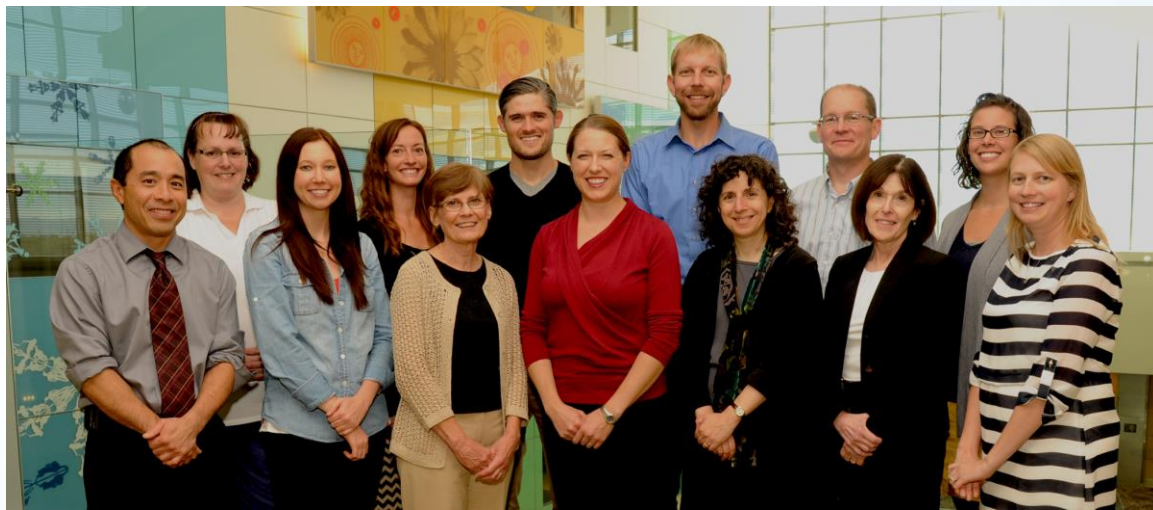
Certified Genetic Counselor

Joanna Reeder, LCSW

Social Work

Carrie Rose-Matens

RMRA Representative





Our Team:

Who is missing?

- Ophthalmology (Neurology)
- Gynecology
- Movement specialist (Neurology)
- Immunologist (Pulmonary)
- Sleep (Neurology, Pulmonary, Development/Behavior)
- Other?



Research Questions, Specific Aims and Hypotheses and Issues



- Questions (not exclusive) to determine standards of care:
 - What is the natural history?
 - What are the associated features?
 - What predicts natural history?
 - Epilepsy?
 - Biomarkers?
 - Specific mutations?
 - How does this impact families?
 - How can we positively affect this?
 - What are the best treatments?



Research Questions, Specific Aims and Hypotheses and Issues



Specific Aims and Hypotheses

1. Longitudinal and very structured evaluations can define the natural history of CDKL5 syndromes. We will perform structured clinical evaluations in our CDKL5 patients.
2. Structured laboratory (MRI, EEG, etc) data collection obtained from clinical evaluations will define biomarkers that can predict clinical course. We will collect structured laboratory data in our CDKL5 patients.
3. A defined natural history is necessary to determine the efficacy of future clinical trials. We will serve as sites for future clinical trials.

Research Questions, Specific Aims and Hypotheses and Issues



Approach (IRB approved):

- Implement structured clinical questionnaire
 - REDCAP
 - Must address research questions, amenable to statistics/quantitative
 - Efficient
 - Patient elements completed during “standard visit”
 - Family elements complete but not overly burdensome
 - Perfect not enemy of good
 - Review of outside records (EEG, MRI, genetics, etc)
 - Completed outside of clinic
- Common, shared international data instrument, single database (or multiple linked dbs)
 - Governance, ownership, authorship, IRBs, standardization
 - Collaboration/Confederation/Federation





Issues

- Threading together the data across sites
- New sites/collaborations
- New questions/adding to the forms/circling back
- Similar/dissimilar approaches
- Time
 - Record review especially EEG review (not just reports)
 - Data entry, analysis



Emerging standards of care: Quick view



- Multidisciplinary team; every 1-2 years
 - Convenient, accessible, interested
- Genetic consultation and counseling
 - Missense mutations: parental confirmation
- Yearly EKG (looking for prolonged QTc)
 - Referral, prolonged/halter if abnormal
- Yearly clinical spine evaluation; every 6 months if abnormal
 - Imaging if abnormal; referral to orthopedics if > 10deg; correction > 30-40deg
- Prolonged EEG; sleep studies
 - For new spell types, evolving spell types; sleep issues
- Therapies
 - Lifelong, Multifaceted
 - Accommodations for visual impairment in the classroom
- Bone health (Vitamin D 400-800U/calcium/day)
- Regular dental exams; regular eye exams
- GYN health

Rett Program Recommendations Childhood Through Adulthood	RETT	CDKL5	FOXP1	MECP2 Duplication
Cardiac Evaluations	<ul style="list-style-type: none"> EKG every 1-2 Years Cardiology referral for any abnormality 	<ul style="list-style-type: none"> EKG every 1-2 Years Cardiology referral for any abnormality 	<ul style="list-style-type: none"> EKG every 1-2 Years Cardiology referral for any abnormality 	<ul style="list-style-type: none"> EKG every 1-2 Years Cardiology referral for any abnormality
Spine evaluations	<ul style="list-style-type: none"> Yearly Physical Exam after age 4yo Upright (sitting or standing) Spine x-ray imaging if curvature appears, then Physical Exam every 6 months until stable through puberty Orthopedics referral for curvature >10 degrees If corrected, yearly Physical Exam 	<ul style="list-style-type: none"> Yearly Physical Exam after age 4yo Upright (sitting or standing) Spine x-ray imaging if curvature appears Orthopedics referral for curvature >10 degrees If corrected, yearly Physical Exam 	<ul style="list-style-type: none"> Yearly Physical Exam after age 4yo Upright (sitting or standing) Spine x-ray imaging if curvature appears Orthopedics referral for curvature >10 degrees If corrected, yearly Physical Exam 	<ul style="list-style-type: none"> Yearly Physical Exam after age 4yo Upright (sitting or standing) Spine x-ray imaging if curvature appears Orthopedics referral for curvature >10 degrees If corrected, yearly Physical Exam
Vitamin D and calcium supplements Vitamin D Level Nutritional assessments	<ul style="list-style-type: none"> At least 400-800 U Vitamin D and calcium daily Follow levels yearly BMI 	<ul style="list-style-type: none"> At least 400-800 U Vitamin D and calcium daily Follow levels yearly BMI 	<ul style="list-style-type: none"> At least 400-800 U Vitamin D and calcium daily Follow levels yearly BMI 	<ul style="list-style-type: none"> At least 400-800 U Vitamin D and calcium daily Follow levels yearly BMI
Eye and Dental Exams	<ul style="list-style-type: none"> Regular Eye exams Dental exams every 6 months/as needed 	<ul style="list-style-type: none"> Yearly Eye exams Dental exams every 6 months/as needed 	<ul style="list-style-type: none"> Yearly Eye exams Dental exams every 6 months/as needed 	<ul style="list-style-type: none"> Regular Eye exams Dental exams every 6 months/as needed
Therapies	<ul style="list-style-type: none"> Lifelong PT(ranging from 1-2x/week- 1x/month) AAC assessment Occupational Therapy Regular seating assessments 	<ul style="list-style-type: none"> Lifelong PT (ranging from 1-2x/week- 1x/month) Vision therapy if needed AAC assessment Occupational Therapy Regular seating assessments 	<ul style="list-style-type: none"> Lifelong PT(ranging from 1-2x/week- 1x/month) Vision therapy if needed AAC assessment Occupational Therapy Regular seating assessments 	<ul style="list-style-type: none"> Lifelong PT (ranging from 1-2x/week- 1x/month) AAC assessment Occupational Therapy
Other	<ul style="list-style-type: none"> Regular Vaccines including Flu Boosters in adolescence and adulthood 	<ul style="list-style-type: none"> Regular Vaccines including Flu Boosters in adolescence and adulthood 	<ul style="list-style-type: none"> Regular Vaccines including Flu Boosters in adolescence and adulthood 	<ul style="list-style-type: none"> Regular Vaccines including Flu Boosters in adolescence and adulthood Immunologist referral



Summary

IFCR: COE

- Diagnostic and therapeutic support for patients and families
- Clinical tools/Future publications
- Emerging standards of care

Special Thanks!!!

Tristen Dinkel
Scott Demarest
Margarita Saenz
Gina VanderVeen
Rett Clinic Team

Our patients and families

IFCR-COE collaborators:

Heather Olson, Sumit Parikh, Walter Kaufmann, Elia Pestana-Knight

NHS-Natural History Study:

Eric Marsh, Alan Percy, Jeff Neul, Alex Paciorkowski, Laura Mamounas, Tim Roberts, Chuck Nelson, Sar Peters, Michaela Fagiolini, etc

Rocky Mountain Rett Association

Ponzo Family Chair in Neuroscience
Research

A large, stylized orange question mark is the central focus of the image. It is surrounded by several smaller, solid-colored circles: a green circle and a blue circle at the top, and a purple circle and an orange circle at the bottom. The word "questions" is written in a simple, orange, sans-serif font across the middle of the question mark's stem.

questions