On the Right Pathway
NF/Ras Pathway Genetics Clinic offers comprehensive care for patients with neurofibromatosis and other RASopathies

Neurofibromatosis type I (NF1) is one of the most common inherited congenital disorders caused by a single gene, affecting approximately one in 3,000 people. In addition to the many clinical conditions associated with NF1 — cardiac abnormalities, vasculopathies, epilepsy and learning disorders, to name a few — evidence shows that it is truly a cancer-prone syndrome as well. Individuals with NF1, for example, harbor a 10 percent lifetime risk of developing a highly aggressive spindle cell sarcoma.

As home to the only academic medical center-based NF clinic in Northern California, UCSF was the first institution in the world to develop a new clinical model for patients who have been diagnosed with NF1 and syndromes related to NF1, which are caused by germline mutations in genes encoding components of the Ras/mitogen activated protein kinase (MAPK) pathway. This clinic is a model not only for the care of patients with Ras pathway disorders (also known as RASopathies), but also for other genetic syndromes.

A leading expert on the clinical implications of these germline mutations, Katherine Rauen, MD, PhD, who founded the clinic in 2007, has seen firsthand the role these mutations play in neurofibromatosis and many other inherited genetic syndromes, including Noonan, CFC, Legius, Costello and others. However, like a traditional NF clinic, individuals with NF2 and schwannomatosis are also seen. Because of the underlying pathogenetic overlap, these syndromes have a predisposition to several types of cancers.

“Because of multisystem involvement, possible malignancies and resulting specialty care needs, providing comprehensive care for these individuals is a challenge,” says Rauen. To meet that challenge, the NF/Ras Pathway Genetics Clinic offers comprehensive case management, prenatal and obstetric care, and multidisciplinary referrals to a network of more than 60 UCSF specialists in adult and pediatric medicine. And because these syndromes are lifetime afflictions, the clinic also facilitates the transition from pediatric to adult care.

After a phone intake that includes a complete medical history and family tree, a patient’s first visit is with Dr. Rauen as a genetics fellow and a genetic counselor, all of whom review the history and conduct a thorough physical exam. “We look for phenotypic markers that form a recognizable pattern of dysmorphology,” says Rauen. “A skin manifestation, for example, can help nail down the clinical diagnosis. A molecular diagnosis can confirm the clinical diagnosis and help family members understand the overall impact, including the risk for cancer, and help them make decisions.”

The next step is to tap into the clinic’s extensive network of UCSF subspecialists. “If we have a patient with Noonan syndrome, for example, we know the patient may be more prone to rhabdomyosarcoma and certain brain tumors, so if needed, we begin a workup and call in the appropriate cancer specialists,” says Rauen. “The advantage is a unifying diagnosis that helps providers know what to be mindful of and that facilitates more personalized medicine.”

“We are so fortunate to have such a stellar team of dedicated health care providers for this one-of-a-kind clinic,” says Rauen. “Throughout the process, we work with the family and their primary care provider to create a joint set of goals that include medical guidance and can also include nonclinical issues. We care for the whole person — and, many times, the entire family — and make sure there are no deficiencies in care.”

For more information about the NF/Ras Pathway Genetics Clinic, visit www.ucsfbenioffchildrens.org/NFRas.

When to refer to the NF/Ras Pathway Genetics Clinic

Because the underlying molecular mechanism in RASopathies is dysregulation of the Ras/MAPK pathway, these conditions exhibit numerous overlapping phenotypic features, including reduced growth, characteristic facial features, cardiac defects, cutaneous abnormalities, neurocognitive delay and a predisposition to neoplasia, both benign and malignant. Clinical indicators for a RASopathy include early onset cancer, café-au-lait macules, freckling, history of cardiac abnormalities (especially pulmonic stenosis), mild hypertrophic cardiomyopathy, short stature and history of mild learning difficulties.

Additional Resources:
- UCSF Osher Center for Integrative Medicine
  Phone: (415) 353-7700
  Website: www.ucsfhealth.org/ocim
- Cancer Risk Program
  Phone: (415) 885-7779
  Website: www.ucsfhealth.org/cancerriskprogram
- Symptom Management Service
  Phone: (415) 885-7671 [885-SMS1]
  Website: cancer.ucsf.edu/sms

Katherine Rauen, MD, PhD, founder and director of the NF/Ras Pathway Genetics Clinic.

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Skeletal muscle cells grown in culture show that Ras G12S (right) do not differentiate normally. Whereas muscle cells with an activated mutant allele into normal multi-nucleated skeletal muscle, whereas muscle cells with an activated mutant Ras G12S (right) do not differentiate normally.
Physician Liaison Service
Phone: (800) 444-2559
Fax: (415) 353-4395
Email: referral.center@ucsfmedctr.org
Contact the Physician Liaison Service for help in making a referral, assistance in obtaining follow-up information or to address other questions or concerns.

Transfer Center
Phone: (415) 353-9166
Fax: (415) 353-9172
The Transfer Center is staffed 24 hours daily to coordinate the transfer of patients to UCSF Medical Center. The center provides quick access to our doctors and other members of our team. We evaluate the needs of each patient to ensure that appropriate care is provided. The center can also facilitate your patient’s return transfer.

Ida & Joseph Friend Cancer Resource Center
Phone: (415) 885-3693
Website: cancer.ucsf.edu/crc
The Cancer Resource Center (CRC) provides patients and their loved ones with information, classes, support groups and referrals to community resources. Most CRC programs are free.

Continuing Medical Education
Phone: (415) 476-4251
Fax: (415) 476-0318
Website: www.cme.ucsf.edu

Information for Health Professionals
Website: www.ucsfhealth.org/healthprofessionals
Our website for health professionals provides information regarding referrals, transfers, billing, consultations, insurance issues and more.

Clinical Trials
Phone: (877) 827-3222
Email: communications@cc.ucsf.edu
Clinical trials database: cancer.ucsf.edu/trials
As home to one of the nation’s largest cancer clinical trials programs, we offer trials focusing on treatment, prevention, survivorship and quality of life. Review our database to find studies for which your patients may be eligible. To subscribe to a monthly email listing of open trials, send your name and email address to clinicaltriallist@ucsfmedctr.org.

NF/Ras Pathway Genetics Clinic
Phone: (415) 476-2757
Fax: (415) 476-9305
Website: www.ucsfbenioffchildrens.org/nFras
The clinic provides comprehensive prenatal, pediatric and adult care management for patients who have, or who are at risk for, a germline ras pathway disorder and offers referring physicians information and support to optimize care so that they may provide a comprehensive family history and guide patients who are at risk for genetic overlap with the NF/Ras Pathway. The clinic also provides a center for genetic counseling and education.

Continuing Medical Education
Phone: (415) 476-4251
Fax: (415) 476-0318
Website: www.cme.ucsf.edu

Information for Health Professionals
Website: www.ucsfhealth.org/healthprofessionals
Our website for health professionals provides information regarding referrals, transfers, billing, consultations, insurance issues and more.

Clinical Trials
Phone: (877) 827-3222
Email: communications@cc.ucsf.edu
Clinical trials database: cancer.ucsf.edu/trials
As home to one of the nation’s largest cancer clinical trials programs, we offer trials focusing on treatment, prevention, survivorship and quality of life. Review our database to find studies for which your patients may be eligible. To subscribe to a monthly email listing of open trials, send your name and email address to clinicaltriallist@ucsfmedctr.org.