TheNetworkEdge

The NF Network presents a periodic research review
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***The Network Edge* brings you regular updates on the latest neurofibromatosis (NF) research and clinical advances from recent scientific publications. *The Network Edge* is organized into "bite sized" sections by specific subtopic, so you can focus on the information that interests you most.**

The Network Edge features…

- The Bottom Line: Each section starts with a **summary sentence** highlighting the "take home" points.

- Federally-Funded Research: All research identified as being either fully or partly funded by the Congressionally Directed Medical Research Neurofibromatosis Research Program (CDMRP NFRP) or the National Institutes of Health (NIH) is **tagged** CDMRP or NIH after the author name.

- A Global NF Picture: To keep you abreast of all NF research advances, *The Network Edge* includes publications from around the world. **Country of the research study** is indicated after the author name.

- *The Network Edge* Archive: At the end of this volume of *The Network Edge*, there is a table showing topics covered by past volumes. This should help if you wish to search for further information in *The Network Edge* archive.

- FREE Publications: Many scientific publications are now available at no charge. These are tagged in the text as FREE. To download full articles, use the embedded links in the references section of this PDF or visit www.pubmed.gov and "search" for the publication title, then follow the links to download.

Highlights from Volume 22 of *The Network Edge*:

- **NF1 MPNSTs:** Researchers discover genomic signatures of MPNSTs that could hopefully be used one day to predict an individual's prognosis and response to treatment using only a blood test.
- **NF1 Learning Disabilities**: Certain executive functioning skills are linked with academic performance over time in children with NF1.
- **NF1 Clinical Management:** Free papers share European clinical guidelines for NF1-related tumor surveillance and resources for adolescents transitioning from pediatric to adult care settings.
- **NF1 Biology:** Combining MEK inhibitors like selumetinib and mirdametinib with other medications may lead to more effective treatment options for plexiform neurofibromas and MPNSTs.
- **NF2 Clinical Trials**: Using a lower dose of bevacizumab for long-term maintenance treatment is effective at controlling tumor size and preserving hearing, and safer than standard doses.
- **NF2 Biology**: Ubiquitin proteasome pathway inhibitor medications such as ixazomib show promising preclinical testing results against schwannomas and meningiomas.
- **Schwannomatosis**: New mouse model of schwannomatosis using patient tumor tissue shows that blocking IL-6 can reduces pain, supporting a soon-to-launch clinical trial testing siltuximab and other medications for treatment of schwannomatosis-related pain.
- **Quality of Life:** A review of previously published papers summarizes psychological and social difficulties of NF1, as well as protective factors and coping strategies used by people with NF1.

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1. NF1 Malignant Peripheral Nerve Sheath Tumors (MPNSTs)

The Bottom Line: Researchers discover genomic signatures of MPNSTs that could hopefully be used one day to predict an individual's prognosis and response to treatment using only a blood test.

Malignant peripheral nerve sheath tumors (MPNSTs) are aggressive cancers that occur in approximately 10% of people with NF1, and can develop when a pre-existing internal neurofibromas transforms from benign to malignant. **Cortes-Ciriano et al**. FREE (United States, Canada, United Kingdom) analyzed how MPNSTs evolve by sequencing the genome of 95 tumor samples. The study found that loss of certain genes, including NF1, CDKN2A, and TP53, led to extensive changes in the tumor's DNA which are associated with different pathways of tumor evolution. The study also found that specific changes in the tumor's DNA are associated with individuals' prognosis and may predict their response to treatment. Because these DNA changes are measurable via blood tests that can detect very small amounts of tumor DNA circulating in a person's bloodstream, the researchers hope to be able to one day to perform these genomic analyses of MPNSTs via a blood test as soon as patients are diagnosed. Once the tumor's unique genetic markers are identified, it could help clinicians understand patients' prognosis and hopefully one day, assign them to more targeted treatment protocols based on their tumor's genetic findings.

2. NF1 Learning Disabilities, Cognition, and School Performance

The Bottom Line: Certain executive functioning skills – such as working memory, cognitive flexibility, and inhibitory control – are linked with academic performance over time in children with NF1. Targeted interventions addressing these skills could help mitigate learning difficulties in kids with NF1 in the future.

Hou et al. NIH, CDMRP (United States) looked at how executive functioning skills (the higher-level cognitive skills that help us plan and execute our goals) relate to academic achievement in children with NF1 and plexiform neurofibromas. The researchers followed 88 children with plexiform neurofibromas over a period of 6 years, testing their executive functioning and academic skills three times. They found that some executive functioning skills, like cognitive flexibility and working memory, were linked to better initial scores on math, reading, and writing tests. They also found that children with lower initial levels of inhibitory control (the ability to stop oneself from doing something) were more likely to experience a decline in reading scores over time. This effect was more pronounced in younger children than in older children, meaning that poor inhibitory control may be a risk factor for declining reading performance, especially in younger children with NF1. The authors hope that better understanding the cognitive factors that contribute to academic problems will allow researchers to design better interventions to remediate learning difficulties and improve the quality of life of children with NF1.

3. NF1 Gliomas (Brain Tumors)

The Bottom Line: Non-optic pathway gliomas in adults with NF1 are often aggressive and difficult to treat based on their location and genetic markers. Even though these tumors are relatively rare, more research into the biology of these tumors is urgently needed to discover better treatments.

People with NF1 have a higher risk of developing brain tumors called gliomas than people without NF1. Most commonly, gliomas occur in children with NF1 along their optic pathway, but adults with NF1 who can also develop gliomas in other parts of their brain. To learn more about what happens to adults with these tumors, **Romo et al**. (United States) analyzed data from 45 adults with NF1 and non-optic pathway gliomas seen at three major medical centers in the US between 1990-2020. The study found that these tumors often have an unexpectedly aggressive clinical course, even when they are low-grade (i.e., when they have features under the microscope that are typically associated with more benign tumors). This may be because most of the tumors were in the midline of the brain and couldn't be removed with surgery, and because all the tumors were IDH1/2 wild-type (a genetic marker that is often seen in harder to treat, malignant brain tumors). After being diagnosed with these tumors, the people in this study lived for an average of 24 months, but this ranged widely from 2 months to 22 years. The study highlights the urgent need for more research on the biology of non-optic pathway gliomas in NF1 so that we can discover better treatments for adults with these tumors.

4. NF1 Clinical Management

The Bottom Line: Free papers share clinical guidelines for identifying and monitoring tumors in people with NF1, and resources for adolescents and young adults with NF1 transitioning from pediatric to adult care settings.

Carton et al. FREE (Belgium, United Kingdom, Spain, Germany, Austria, Finland, Sweden, the Netherlands) share guidelines for caring for people with NF1 developed by the European Reference Network on Genetic Tumor Risk Syndromes. After conducting a review of published research on NF1, a group of NF1 experts from across Europe discussed and voted on clinical recommendations to care for people with NF1, with a focus on how to best identify and monitor the many types of benign and cancerous tumors that people with NF1 may develop. While these recommendations provide evidence-based suggestions for what medical care individuals with NF1 need, the authors note that all decisions about an individual's healthcare should be made in concert with their personal physicians to adjust to their unique circumstances. The full paper, which is available for free, has specific screening suggestions for plexiform neurofibromas, cutaneous neurofibromas, optic pathway and other gliomas (brain tumors affecting the visual pathway or other areas of the brain), malignant peripheral nerve sheath tumor (MPNST), breast cancer, juvenile leukemia (a blood cancer that occurs rarely in children), pheochromocytoma (a tumor of the adrenal gland on top of the kidney), gastrointestinal stromal tumors (a tumor in the digestive tract), and glomus tumors (small benign tumors in the fingers and toes).

Radtke et al. FREE (United States) wrote an overview of issues related to helping adolescents and young adults with NF1 start to take over more of their own healthcare decision-making from their parents, and move from pediatric to adult clinics. The authors also recommend that NF1 clinics develop formal healthcare transition programs to help their patients build independence, improve their quality of life, and identify and treat NF1-associated medical complications as they age. These programs should include a focus on building health-related self-management skills, providing psychosocial support and referrals, connecting patients with resources to obtain accommodations at school and work, and making sure they have access to genetic counseling for family planning when needed. The article also includes links to a number of general and NF1-specific resources to help prepare adolescents and young adults to manage their own healthcare that can be freely accessed by NF1 families and physicians.

5. NF1 Bony Abnormalities

The Bottom Line: People with NF1 who require multi-level fusion surgery for their scoliosis may have more neurologic and pulmonary issues after surgery than people without NF1 undergoing this surgery, but overall they have similar complications and mortality rates as people without NF1.

Price et al. (United States) looked at the outcomes of multilevel fusion surgery for NF1 patients with scoliosis, and compared the results to people without NF1 undergoing the same procedure in a large national database. Multilevel fusion surgery may be recommended for scoliosis when the curvature of the spine is severe and causing pain or other symptoms, such as difficulty breathing or limited mobility. The goal of this surgery is to straighten the spine and stabilize it by fusing two or more vertebrae together using bone grafts, screws, and metal rods. The researchers found that patients with NF1 were more likely to have other health problems, such as high blood pressure and clinical depression, than other people undergoing this surgery. After surgery, NF1 patients had a higher incidence of some complications, such as seizures (which occurred in 5.7% of people with NF1) and hydrocephalus (extra fluid in the brain, which occurred in 1.9% of people with NF1). However, people with NF1 had the same overall complication rates and risk of death as people without NF1 (and in fact, none of the 533 patients with NF1 died during their hospital stay.) These findings suggest that surgeons should be aware of the increased risk factors for NF1 patients undergoing multilevel fusion surgery, but overall, the surgery is relatively safe when done by experienced surgeons.

6. NF1 and Autism

The Bottom Line: On average, preschool age kids with NF1 have different eye movement patterns then typically developing kids, which likely reflect differences in attention that may lead to symptoms of autism. Future research could study these eye movements to see if they predict which children will go on to develop autism spectrum disorder.

Hocking et al. (Australia, United States) looked at the ability of preschoolers with NF1 to habituate, or get used to repetitive information, when looking at visual stimuli. The researchers used a new eye-tracking technique to measure this habituation ability and compared the results of children with NF1 to those with Autism Spectrum Disorder (ASD) and typically developing children. The study found that children with NF1 had difficulty habituating to repeating stimuli compared to typically developing kids – that is, they looked longer at repeating visual images instead of moving on to the new images. On average, the more a child with NF1 had difficulty in habituating to repetitive images, the higher the level of ASD traits they displayed. This may be due to differences in attentional networks in people with NF1, and may also help explain the emergence of ASD symptoms in some children with NF1. The authors recommend doing further studies using eye-tracking in children over time to see if the technique can help predict whether preschoolers with NF1 will go on to develop ASD or learning issues in the future.

7. What's New in NF1 Biology?

The Bottom Line: Promising data in mouse models suggests that combining MEK inhibitors with other medications may lead to more effective treatment options for plexiform neurofibromas and MPNSTs.

Selumetinib has been approved for the treatment of inoperable plexiform neurofibromas in children with NF1, but it does not completely get rid of tumors or work for 100% of people with NF1. **Jackson et al.** [FREE] (United States, Austria) are testing whether combining selumetinib with other medications might make it more effective at treating plexiform neurofibromas. The researchers found that a new drug – a SOS1 inhibitor called BI-3406 – can block an important part of the cell signaling pathway that causes plexiform neurofibromas to grow despite treatment with MEK inhibitors (like selumetinib). This means that treatment combining BI-3406 and MEK inhibitors could potentially have more dramatic effects on tumors than treatment with selumetinib alone, because combined treatments would block more pathways for tumor growth. And when the researchers gave BI-3406 and selumetinib to mice with plexiform neurofibromas, the tumors did shrink even more than they did with selumetinib alone. While more research is needed to see if this drug combination will work in humans, these are promising results towards discovering more effective combination treatments for plexiform neurofibromas.

Malignant peripheral nerve sheath tumors (MPNSTs) occur in about 10% of people with NF1. Since there are limited treatment options beyond surgery for these aggressive tumors, finding effective medical treatments for MPNSTs is a high priority. **Borcherding et al**. [CDMRP] (United States) examined whether drugs inhibiting a protein called TYK2 could be effective at treating MPNSTs. The researchers found that inhibiting TYK2 decreased tumor cell proliferation and induced death in cells, as well as reduced tumor growth in mouse models. These findings suggest that TYK2 could be a potential therapeutic target for NF1-associated MPNST. Furthermore, the researchers found that combining drugs that inhibit TYK2 with drugs that inhibit MEK had even more dramatic results in these preclinical models. Based on these findings, the authors recommend conducting a phase I clinical trial of deucravacitinib (a TYK2 inhibitor) and mirdametinib (a MEK inhibitor) in patients with NF1-assosciated MPNSTs.

8. NF2 Clinical Trials

The Bottom Line: Using a lower dose of bevacizumab over two years of treatment was largely effective at preventing tumor growth and preserving hearing, while likely being safer than standard doses.

Multiple studies have shown that treatment with bevacizumab can improve hearing and help shrink vestibular schwannomas in one-third to one-half of people with NF2. However, bevacizumab can have significant side effects, such as high blood pressure and damage to the kidneys, especially when used at higher doses or for long time periods. For this reason, researchers designed a clinical trial of bevacizumab that used different doses of the medication to try to maximize the drug's efficacy and minimize side effects. The trial involved 20 participants who received bevacizumab for 2 years - a higher dose of bevacizumab for the first 6 months, and a lower dose of bevacizumab for the next 18 months, with the option to go back to a higher dose if their hearing got worse. **Plotkin et al**. [CDMRP, NIH, FREE] (United States) previously showed that using a higher dose of bevacizumab at the start of treatment does not seem to be more effective at shrinking tumors or improving hearing than using a standard dose of bevacizumab.

Now, in a new publication, **Plotkin et al**. CDMRP, NIH (United States) showed that using a lower dose of bevacizumab for long-term maintenance after the initial six months of therapy is effective at preventing hearing loss and tumor growth, and is well-tolerated over two years. All 20 individuals with NF2 had some hearing loss at the start of the trial, but after 48 weeks of treatment, almost all (95%) had not lost any further hearing. After 98 weeks of treatment, 89% of people had stable or shrinking vestibular schwannomas and 70% had stable or improved hearing. Over the two years, 3 of the 20 participants stopped receiving bevacizumab due to side effects. Overall, these papers suggest that lower doses of bevacizumab are likely to be just as efficacious and even safer than standard or high dose therapy.

9. NF2 Clinical Management

The Bottom Line: Stereotactic radiosurgery is often safe and effective at stopping the growth of vestibular schwannoma, although it is less successful at preserving hearing long-term.

Bin-Alamer et al. (United States, Canada, Egypt, Turkey, Taiwan, India, Czech Republic, Spain, Dominican Republic) studied the use of stereotactic radiosurgery (SRS) to treat vestibular schwannomas in 267 people with NF2 seen in 12 hospitals across the world. They found that SRS treatment helped limit tumor growth in most patients. At 10 years after treatment, only 23% of people had their tumor grow and only 15% needed additional treatment for their tumor. However, hearing loss was still common, with only 35% of patients having useful hearing at 10 years post-treatment. The researchers did not find any cases of new tumors or cancer caused by the treatment in the patients they studied. Overall, the study suggests that SRS can be an effective treatment to control vestibular schwannoma growth in people with NF2.

10. What's New in NF2 Biology?

The Bottom Line: Ubiquitin proteasome pathway inhibitor medications such as ixazomib show promising preclinical testing results against schwannomas and meningiomas; researchers discover a biological reason why schwannomas develop and behave differently despite having the same genetic mutations.

Bhattacharyya et al. CDMRP, NIH (United States) tested three drugs that target the ubiquitin-proteasome pathway (UPP), which is involved in the breakdown of proteins in cells, to see if they could be used to treat NF2-related meningiomas and schwannomas. The drugs ixazomib and TAK-243 were found to be effective in reducing the growth of meningioma and schwannoma cells in preclinical models, while the drug pevonedistat was not effective. The researchers also mapped out what proteins were increased and decreased in the tumor cells after treatment to help explain how these drugs work. These results suggest that UPP inhibitor medications could be a promising new treatment option for NF2 patients.

Virtually all schwannomas are caused by problems with the *NF2* gene, with very few other genetic changes. Despite this, schwannomas can behave very differently from each other, which makes it difficult to predict which tumors need treatment at what time. **Chiasson-MacKenzie et al**. CDMRP, NIH FREE (United States) studied why schwannomas are so variable and discovered that the problem comes from a part of the NF2 protein that is involved in helping cells keep their shape, stay in the right place, and communicate with neighboring cells. When the *NF2* gene isn't working properly, this function is impaired and cells must each develop new and different ways of communicating with each other. This helps explain why

schwannomas display different behavior even though they have genetically similar problems. The researchers then developed a new technique to precisely measure this biological process in mouse models of NF2, which can be hopefully used to better understand the biology of schwannomas and one day better predict tumor behavior in people to guide their treatment strategies.

11. Schwannomatosis Update

The Bottom Line: Blocking IL-6 reduces pain in new mouse model that uses transplanted tumor tissue from schwannomatosis patients; results support an upcoming clinical trial testing the anti-IL6 antibody siltuximab and other medications for pain reduction in adults with schwannomatosis.

Schwannomatosis can causes chronic and debilitating pain, for which there is currently no particularly effective medical treatment. While the relationship behind pain and tumor growth in schwannomatosis is not fully explained, it has been observed that pain is not always related to tumor size and is not always relieved by tumor removal. This suggests that there may be other causes for pain besides nerve compression from tumors. Unfortunately, research into schwannomatosis-related pain had been limited by the lack of relevant preclinical research models.

For this reason, **Yin et al.** FREE, NIH, CDMRP (United States) established new schwannomatosis research models called patient-derived xenografts, where tumor tissue from a schwannomatosis patient is transplanted into a mouse, allowing the tumor to grow and behave in way that closely mimics the human body. The researchers successfully did this with tumor samples from 9 people with schwannomatosis, including some who had pain and some who did not. Using these models, they were able to discover more about the biological mechanisms behind schwannomatosis pain and schwannoma growth. Specifically, they found that schwannomas on peripheral nerves cause macrophages to enter the dorsal root ganglia, and these macrophages cause pain by producing too much interleukin-6 (IL-6). Blocking IL-6 reduces pain but has only limited effects on tumor growth, potentially due to epidermal growth factor (EGF) signaling that occurs when IL-6 is blocked. However, blocking both IL-6 and EGF simultaneously controlled pain and tumor growth in these xenograft models of SWN.

These findings have led to testing of an anti-IL6 antibody medication called siltuximab in a clinical trial for pain in patients with schwannomatosis. The Screening Trial for Pain Relief in Schwannomatosis (STARFISH) at Massachusetts General Hospital is a platform trial designed to be able to test multiple pain medications in adults with schwannomatosis. Currently, there are two pain medications planned for testing – siltuximab and erenumab, a CGRP receptor antibody - and more medications may be added as additional preclinical evidence is gathered to identify additional treatment options. The trial was not yet open to recruitment at the time this issue was completed (April 2023), but details of the trial and updates regarding recruitment will be available at https://clinicaltrials.gov/ct2/show/NCT05684692

Note: This paper has been published online as a preprint, meaning it has not yet been reviewed by independent scientists or published in a biomedical journal. As such, the content in the final published paper may be slightly different than in this article. Because the National Library of Medicine if running a pilot program to share the results of NIH-funded research earlier to the public by including preprint articles, we have also shared a summary of this article prior to its publication in a traditional journal.

12. Quality of Life and Mental Health in NF1, NF2, and Schwannomatosis

The Bottom Line: Suicidal thoughts are not uncommon in people with all types of NF who sign up for psychosocial clinical trials, so clinicians should routinely offer support and resources to patients; a review of previously published papers summarizes psychological and social difficulties of NF1, as well as protective factors and successful coping strategies used by people with NF1.

Lester et al. CDMRP (United States) looked at how often people with all forms of neurofibromatosis think about suicide and what factors might be related to those thoughts. The researchers surveyed 220 adults with NF1, NF2, and schwannomatosis who signed up to participate in a clinical trial of a mind-body resiliency program, and asked about their mental health, stress, pain, and overall quality of life. They found that 19% of people who signed up for this clinical trial reported having suicidal thoughts (i.e., When asked how often they had thoughts they would be better off dead or of hurting themselves in some way in the past 2 weeks, they selected "several days", "more than half the days", or "nearly every day" instead of "not at all"). Participants with NF2 were more slightly more likely to report suicidal thoughts compared to participants with NF1 or schwannomatosis, and across diagnoses, people with depression or poor psychological quality of life were at the highest risk of having suicidal thoughts. The researchers suggest that healthcare providers who work with people with NF should be aware of these concerns and provide support and resources when needed. It is also important for people with NF to know that these thoughts are not uncommon and that help is available if they are experiencing them.

Hocking et al. FREE (France) conducted a systematic review of published research papers on the psychosocial impact of rare, genetic diseases that affect the skin, including neurofibromatosis 1. They found 16 studies on NF1, that included a total of 1180 participants, mostly from the U.S. and Europe, and summarized their findings. Many families with NF1 report receiving insufficient information or counseling about NF1, and one study showed that people's self-esteem was higher if they received care at a NF clinic or had received genetic counseling. Many (but not all) people with NF1 were anxious or fearful of passing the disease onto their children; referral to genetic counseling, preconception services, and/or prenatal testing could help address these worries. People with NF1 may have increased difficulty in social relationships, including being stigmatized or bullied because of their appearance and experiencing anxiety surrounding romantic/sexual relationships. Studies suggest seeking additional support from one's family and close friends to compensate for these difficulties is helpful, and one study found that people's self-esteem was higher if they had friends with NF1 or attended an NF1 support group. People with NF1 commonly reported cosmetic issues that could cause problems with self-esteem and body image, cognitive difficulties, mental health problems, and worries about the unpredictable course of their disease. Different ways people successfully coped with this included accepting NF1 as a life-long disorder, gaining more knowledge about NF1 to feel more empowered to manage their condition, and focusing on spirituality or other values that supporting a sense of community and purpose.

The Network Edge Archive

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References

Bhattacharyya S, Oblinger JL, Beauchamp RL, Yin Z, Erdin S, Koundinya P, Ware AD, Ferrer M, Jordan JT, Plotkin SR, Xu L, Chang LS, Ramesh V. Proteasomal pathway inhibition as a potential therapy for NF2-associated meningioma and schwannoma. Neuro Oncol. 2023 Feb 20:noad037. Online ahead of print.

Bin-Alamer O, Faramand A, Alarifi NA, Wei Z, Mallela AN, Lu VM, Nabeel AM, Reda WA, Tawadros SR, Abdelkarim K, El-Shehaby AMN, Emad RM, Peker S, Samanci Y, Lee CC, Yang HC, Delabar V, Mathieu D, Tripathi M, Kearns KN, Bunevicius A, Sheehan JP, Chytka T, Liscak R, Moreno NM, Álvarez RM, Grills IS, Parzen JS, Cifarelli CP, Rehman AA, Speckter H, Niranjan A, Lunsford LD, Abou-Al-Shaar H. Stereotactic Radiosurgery for Vestibular Schwannoma in Neurofibromatosis Type 2: An International Multicenter Case Series of Response and Malignant Transformation Risk. Neurosurgery. 2023 Mar 2. Online ahead of print.

Borcherding DC, Amin NV, He K, Zhang X, Lyu Y, Dehner C, Bhatia H, Gothra A, Daud L, Ruminski P, Pratilas CA, Pollard K, Sundby T, Widemann BC, Hirbe AC. MEK inhibition synergizes with TYK2 inhibitors in NF1-associated Malignant Peripheral Nerve Sheath Tumors. Clin Cancer Res. 2023 Feb 17:CCR-22-3722. Online ahead of print.

Carton C, Evans DG, Blanco I, Friedrich RE, Ferner RE, Farschtschi S, Salvador H, Azizi AA, Mautner V, Röhl C, Peltonen S, Stivaros S, Legius E, Oostenbrink R; ERN GENTURIS NF1 Tumour Management Guideline Group. ERN GENTURIS tumour surveillance guidelines for individuals with neurofibromatosis type 1. EClinicalMedicine. 2023 Jan 13;56:101818.

Chiasson-MacKenzie C, Vitte J, Liu CH, Wright EA, Flynn EA, Stott SL, Giovannini M, McClatchey AI. Cellular mechanisms of heterogeneity in NF2-mutant schwannoma. Nat Commun. 2023 Mar 21;14(1):1559.

Cortes-Ciriano I, Steele CD, Piculell K, Al-Ibraheemi A, Eulo V, Bui MM, Chatzipli A, Dickson BC, Borcherding DC, Feber A, Galor A, Hart J, Jones KB, Jordan JT, Kim RH, Lindsay D, Miller C, Nishida Y, Proszek PZ, Serrano J, Sundby RT, Szymanski JJ, Ullrich NJ, Viskochil D, Wang X, Snuderl M, Park PJ, Flanagan AM, Hirbe AC, Pillay N, Miller DT; Genomics of MPNST (GeM) Consortium. Genomic Patterns of Malignant Peripheral Nerve Sheath Tumor (MPNST) Evolution Correlate with Clinical Outcome and Are Detectable in Cell-Free DNA. Cancer Discov. 2023 Mar 1;13(3):654-671.

Fournier H, Calcagni N, Morice-Picard F, Quintard B. Psychosocial implications of rare genetic skin diseases affecting appearance on daily life experiences, emotional state, self-perception and quality of life in adults: a systematic review. Orphanet J Rare Dis. 2023 Feb 23;18(1):39.

Hocking DR, Sun X, Haebich K, Darke H, North KN, Vivanti G, Payne JM. Delineating Visual Habituation Profiles in Preschoolers with Neurofibromatosis Type 1 and Autism Spectrum Disorder: A Cross-Syndrome Study. J Autism Dev Disord. 2023 Mar 6. Epub ahead of print.

Hou Y, Wu X, Allen T, Toledo-Tamula MA, Martin S, Gillespie A, Goodwin A, Widemann BC, Wolters PL. Longitudinal association between executive function and academic achievement in children with neurofibromatosis type 1 and plexiform neurofibromas. J Int Neuropsychol Soc. 2023 Feb 8:1-11.

Jackson M, Ahmari N, Wu J, Rizvi TA, Fugate E, Kim MO, Dombi E, Arnhof H, Boehmelt G, Düchs MJ, Long CJ, Maier U, Trapani F, Hofmann MH, Ratner N. Combining SOS1 and MEK inhibitors in a murine model of plaxiform neurofibroma results in tumor shrinkage. J Pharmacol Exp Ther. 2023 Feb 27. Online ahead of print.

Lester EG, Wang KE, Blakeley JO, Vranceanu AM. Occurrence and Severity of Suicidal Ideation in Adults With Neurofibromatosis Participating in a Mind-Body RCT. Cogn Behav Neurol. 2023 Mar 1;36(1):19-27.

Plotkin SR, Allen J, Dhall G, Campian JL, Clapp DW, Fisher MJ, Jain RK, Tonsgard J, Ullrich NJ, Thomas C, Edwards LJ, Korf B, Packer R, Karajannis MA, Blakeley JO. Multicenter, prospective, phase 2 study of maintenance bevacizumab for children and adults with NF2-related schwannomatosis and progressive vestibular schwannoma. Neuro Oncol. 2023 Apr 3:noad066. Online ahead of print.

Plotkin SR, Duda DG, Muzikansky A, et al. Multicenter, Prospective, Phase II and Biomarker Study of High-Dose Bevacizumab as Induction Therapy in Patients With Neurofibromatosis Type 2 and Progressive Vestibular Schwannoma. J Clin Oncol. 2019;37(35):3446-3454.

Price G, Martini ML, Caridi JM, Lau D, Oermann EK, Neifert SN. A Nationwide Study Characterizing the Risk and Outcome Profiles of Multilevel Fusion Procedures in Neuromuscular Scoliosis Patients with Neurofibromatosis Type 1. World Neurosurg. 2023 Mar;171:e620-e630.

Radtke HB, Berger A, Skelton T, Goetsch Weisman A. Neurofibromatosis Type 1 (NF1): Addressing the Transition from Pediatric to Adult Care. Pediatric Health Med Ther. 2023 Feb 9;14:19-32.

Romo CG, Piotrowski AF, Campian JL, Diarte J, Rodriguez FJ, Bale TA, Dahiya S, Gutmann DH, Lucas CG, Prichett L, Mellinghoff I, Blakeley JO. Clinical, Histological and Molecular Features of Gliomas in Adults with Neurofibromatosis Type 1. Neuro Oncol. 2023 Feb 25. Online ahead of print.

Yin Z, Wu L, Zhang Y, Sun Y, Chen JW, Subudhi S, Ho W, Lee GY, Wang A, Gao X, Ren J, Zhu C, Zhang N, Ferraro GB, Muzikansky A, Zhang L, Stemmer-Rachamimov A, Mao J, Plotkin SR, Xu L. Co-Targeting IL-6 and EGFR signaling for the treatment of schwannomatosis and associated pain. bioRxiv [Preprint]. 2023 Feb 6. doi: 10.1101/2023.02.06.527377.