Neurofibromatosis Research Program Accomplishments
CDMRP Public Affairs: 301-619-7071

Log Number	Principal Investigator	Type	Accomplishment	Relevant Publications
			1996	
NF960003	Friedman	NF1	Established associations between subpopulations of individuals with NF1 and different clinical features.	(1) Lin AE, et al. 2000. Am J Hum Genet 95:108-117. (2) Stevenson DA, et al. 1999. Am J Hum Genet 84(5):413-419. (3) Szudek J, et al. 2000. Am J Med Genet 92:224-228. (4) Szudek J, et al. 2002. Genet Epidemiol 23(2):150-164.
NF960013	Devries	NF1	Demonstrated that neurofibrosarcoma-derived cells overexpress c-kit; drugs inhibiting c-kit activity are being studied in clinical trials.	(1) Badache A and DeVries GH. 1998. J Cell Phys 177:334-342.
NF960018	Ratner	NF1	Developed a nerve wounding model showed that Nf1 mutation in mouse fibroblasts causes abnormalities characteristic of human neurofibromas and a skin carcinogenesis model supporting a role for NF1 in epithelial carcinogenesis.	(1) Atit RA, et al. 2000. J Invest Dermatol 114:1092-1100. (2) Rizvi TA, et al. 2002. J Neurosci 22(22):9831-9840.
NF960027	Wallace	NF1	Identified that the loss of neurofibromin is associated with tumorigenesis.	(1) Muir D, et al. 2001. Am J Pathol 158(2):501-513.
NF960041	Jacks	NF1	Developed first mouse model of NF1-related MPNSTs.	(1) Cichowski K, et al. 1999. Science 286:2172-2176.
NF960043	Stephens	NF1	Identified that interstitial isodisomy was the mechanism of NF1 loss of heterozygosity (loss of one copy of the gene) in some patients. Demonstrated an association of NF1 isodisomy and the development of myeloid malignancies in children with NF1.	(1) Dorschner MO, et al. 2000. Hum Mol Genet 9:35-46. (2) Stephens K, et al. 2006. Blood 108(5):1684-1689.
NF960044	Parada	NF1	Characterized loss of Nf1 in various cell types and demonstrated that loss of Nf1 in the Schwann cell lineage was sufficient to generate tumors.	(1) Zhu Y, et al. 2001. Genes Dev 15(7):859-876. (2) Zhu Y, et al. 2002. Science 296(5569):920-922. (3) Gitler AD, et al. 2003. Nat Genet 33(1):75-79.
NF960051	Brannan	NF1	Identified three loci that may contribute to the progression of NF1-associated juvenile myelomonocytic leukemia (JMML) to acute leukemia.	(1) Blaydes SM, et al. 2001. J Virol 75:9427-9434. (2) Costa RM, et al. 2001. Nature Genetics 27:399-405.
NF960039	MacCollin	NF2	Established associations between types of NF2 mutations and clinical features; also developed novel methods for detecting NF2 mutations.	(1) Hill E, et al. 1998. Am J Hum Geneti 63:1330. (2) MacCollin M, et al. 1998. Sem in Pediatr Neurol 5:234-252. (3) Kluwe L, et al. 2000. Neurogenetics 3(1):17-24. (4) Patronas N, et al. 2001. Radiology 218(2):434-442.
NF960063	Der	NF2	Identified NF2 as a negative modulator of Rac function.	(1) Shaw RJ, et al. 2001. Dev Cell 1(1):63-72.
			1997	
NF970002	Korf	NF1	Established volumetric MRI as the "gold standard" for measuring growth of plexiform neurofibromas.	(1) Young Poussaint T, et al. 2003. Am J Radiol 180:419-423. (2) Dombi E, et al. 2007. Neurology 68:643-647. (3) Lim R, et al. 2005. Am J Roentgenol 184(3):962-968.
NF970001	Slattery	NF2	Established a consortium to study natural history of NF2.	(1) Slattery WH, et al. 2004. Otol Neurotol 25(5):811-817. (2) Slattery WH, et al. 2005. Otol Neurotol 26(4):733-740. (3) Fisher LM, et al. 2009. Otol Neurotol 30(6): 835-841.

Log Number	Principal Investigator	Type	Accomplishment	Relevant Publications
			1998	
NF980012	Zhong	NF1	Demonstrated that Ras stimulates adenyl cyclas activity in an NF1-dependent manner and that this pathway may be involved in mediating growth factor signaling.	(1) Tong J, et al. 2002. Nat Neurosci 5(2)95-96.
NF980004	McClatchey	NF2	Provided insight into the function of the NF2 (merlin) protein, which acts as a tumor and metastasis suppressor by controlling cell-cell contact.	(1) Lallemand D, et al. 2003. Genes Dev 17(9):1090-1100.
			1999	
NF990007	North	NF1	Established that MRI T2 hyperintensities measured in children with NF1 are a good predictor of cognitive dysfunction in adulthood.	(1) Hyman SL, et al. 2003. Neurology 60:1139-1145.
NF990031	Stephens	NF1	Identifed the hotspots were 69% of NF1 microdeletions occur and developed sensitive assays to detect these microdeletions in a blood sample.	(1) López-Correa C, et al. 2001. Hum Mol Genet 10:1387-1392. (2) Jenne DE, et al. 2003. Genes Chrom Can 37:111-120. (3) Forbes SH, et al. 2004. Genes Chrom Can 41:12-25.
NF990044	Cutting	NF1	Demonstrated that children with NF1 have differences in visuospatial processing, inferential language, and retrieval rate that could be used to tailor academic interventions.	(1) Clements-Stephens et al. 2008. Neurophyscholigia 46(2):690-697. (2) Cutting LE et al. 2010. Child Neuropsychol 16(5):417-432.
NF990047	Muir	NF1	Established model of NF1 peripheral nerve tumors.	(1) Muir D, et al. 2001. Am J Pathol 158:501-513.
NF990013	Breakefield	NF2	Used MRI to detect schwannomas in a transgenic murine model of NF2 and demonstrated a decrease in NF2 tumor size following treatment with an oncolytic G47Delta vector.	(1) Messerli SM, et al. 2002. Neoplasia 4:501-509. (2) Prabhakar S, et al. 2007. Cancer Gene Ther 14(5):460-467.
NF990043	Carpen	NF2	Provided evidence for connection between merlin and PKA signaling.	(1) Gronholm M, et al. 2003. J Biol Chem 278:41167-41172. (2) Alfthan K, et al. 2004. J Biol Chem 279(18):18559-18566.
NF990018	Shannon	NF1/2	Developed mouse models of meningioma, schwannoma, and progressive myeloproliferative disorder.	(1) Zhu Y, et al. 2001. Genes Dev 15(7):859-876. (2) Bajenaru ML, et al. 2002. Mol Cell Biol 22(14):5100-5113. (3) Zhu Y et al. 2002. Science 296(5569):920-922. (4) Kalamarides M, et al. 2002. Genes Dev 16(9):1060-1065. (5) Le DT, et al. 2004. Blood 103(11):4243-4250.
NF990038	Joe	NF1/2	Developed and applied novel statistical models to analyze NF1 and NF2 genetic and phenotypic data.	(1) Szudek J, et al. 2002. Genet Epidemiol 23(2):150-164. (2) Zhao Y et al. 2002. Genet Epidemiol 23(3): 245-249. (3) Baser ME, et al. 2003. J Med Genet 40:758-760. (4) Woods R, et al. 2003. Genet Epidemiol 24(4):265-272.

Log Number	Principal Investigator	Type	Accomplishment	Relevant Publications
			2000	
NF000016	Wallace	NF1	Demonstrated that steroid hormones can significantly affect the growth of NF1 tumor cells.	(1) Fishbein L, et al. 2007. Mol Carcinog 46(7):512-523.
NF000027	Widemann	NF1	Performed Phase II clinical trial of oral Tipifarnib in children and adolescents with NF1.	
NF000035	Clapp	NF1	Demonstrated that Nf1-deficient Schwann cells secrete Kit ligand, an activator of c-kit, and this is sufficient to stimulate mast cell migration. Established interactions between different cell types within neurofibromas (Schwann cell-mast cell and fibroblast-mast cell interactions).	(1) Yang FC, et al. 2003. J Clin Invest 112:1851-1861.
NF000015	Slattery	NF2	Characterized growth rates and clinical course of tumors associated with NF2.	(1) Slattery WH, et al. 2004. Otol Neurotol 25(5):811-817. (2) Slattery WH, et al. 2005. Otol Neurotol 26(4):733-740. (3) Fisher LM, et al. 2007. Otol Neurotol 28(8):1083-1090. (4) Harris GJ, et al. 2008. Neurosurg 62:1314-1320. (5) Fisher LM et al. 2009. Otol Neurotol 30(6):835-841.
			2001	
NF010042	Packer	NF1	Performed Phase I and Phase II clinical trials of oral Pirfenidone in children and adolescents with NF1 and plexiform neurofibromas.	(1) Babovic-Vuksanovic D, et al. 2007. Pediatr Neurol 36(5):293-300.
NF010144	Silva	NF1	Demonstrated that lovastatin treatment reverses learning deficits in a Nf1 mouse model.	(1) Costa RM, et al. 2002. Nature 415:526-530. (2) Li W, et al. 2005. Curr Biol 15(21):1961-1967.
NF010097	Gusella	NF2	Identified magician as a binding partner for merlin, suggesting a possible novel role for merlin in cell signaling and cytoskeletal reorganization.	(1) Wiederhold T, et al. 2004. Oncogene 23(54):8815-8825.
NF010093	Shannon	NF1/2	Developed new mouse models for NF1- and NF2-associated tumors.	(1) Gutmann DH, et al. 2003. Cancer Res 63(11): 3001-3004. (2) Leneuve P, et al. 2003. Nucleic Acids Res 31(5):1-8. (3) Weiss BG and Shannon KM. 2004. Preclinical trials in mouse cancer models. In: Mouse Models of Human Cancer (Holland EC, Ed), pp 437-446. Wiley-Liss, Hoboken, New Jersey. (4) Parada LF, et al. 2005. Modeling neurofibromatosis type 1 tumors in the mouse for therapeutic intervention. Cold Spring Harbor Symposia on Quantitative Biology: Molecular Approaches to Controlling Cancer.
NF010096	Gusella	NF1/2	Identified chromosomal imbalances associated with meningiomas.	(1) Nunes F, et al. 2005. Cancer Genet Cytogenet 162(2):135-139.
			2002	
NF020029	Hingtgen	NF1	Demonstrated that sensory neurons from Nf1 mutant mice have enhanced excitability, perhaps due in part to increased Ras activity.	(1) Wang Y, et al. 2005. J Neurophysiol 94:3670-3676. (2) Hingtgen C, et al. 2006. Neuroscience 137:637-645.
NF020033	Cichowski	NF1	Demonstrated that neurofibromin regulates the mTOR pathway through activated Ras.	(1) Johannessen C, et al. 2005. Proc Natl Acad Sci 102(24):8573-8578.
NF020015	MacCollin	Sch	Confirmed mutations in SMARCB1 in familial schwannomatosis.	(1) Boyd C, et al. 2008. 74(4):358-366.

Log Number	Principal Investigator	Type	Accomplishment	Relevant Publications
			2003	
NF030010	Ratner	NF1	Identified SOX9 as an MPNST survival-dependent oncogene and potential biomarker for MPNST.	(1) Miller SJ, et al. 2006. Cancer Res 66(5):2584-2591. (2) Miller SJ, et al. 2009. EMBO Mol Med 1(4):236-248. (3) Miller SJ, et al. 2010. Oncogene 29(3):368-379.
NF030015	North	NF1	Demonstrated that age 2 years may be the appropriate time to perform screen to detect deficits in cognitive and motor function in children with NF1.	(1) Lorenzo J, et al. 2011. J Pediatr 158(4):660-665.
NF030039	Martuza	NF2	Demonstrated that an oncolytic recombinant HSV vector reduces schwannoma tumor volumes in NF2 mouse model.	(1) Messerli S, et al. 2006. Human Gene Therapy 17:20-30.
			2004	
NF043019	Ingram	NF1	Identified VEGF and bFGF as novel molecular targets in neurofibromin-deficient endothelial cells for the treatment of neurofibromas.	(1) Munchhof AM, et al. 2006. Hum Mol Genet 15:1858-1869.
NF043032	Yang	NF1	Demonstrated that the growth factor TGF-beta secreted from mast cells plays a critical role in the initiation and progression of neurofibromas.	(1) Yang F-C, et al. 2006. Hum Mol Genet 16:1-17.
NF043090	Zhong	NF1	Demonstrated that NF1 is involved in both immediate and long-term memory through distinct signaling mechanisms.	(1) Ho IS, et al. 2007. J Neurosci 27(25):6852-6857.
NF043037	Peterson	NF2	Identified the first allosteric small-molecular inhibitors of Pak1.	(1) Deacon SW, et al. 2008. Chem Biol 15:322-331.
NF043040	McClatchey	NF2	Elucidated the mechanistic relationship between NF2 and EGFR, and the role in tumor cell proliferation.	(1) Curto M, et al. 2007. J Cell Biol 177(5):893-903. (2) Cole BK, et al. 2008. Mol Cell Biol 28(4):1274. (3) Gladden AB, et al. 2010. Dev Cell 19(5):727-739.
NF043050	Shannon	NF1/2	Characterized mouse models of NF1 and NF2 to study disease mechanisms and evaluate therapeutic approaches.	(1) McLaughlin ME, et al. 2007. Proc Nat Acad Sci 104(9):3261-3266. (2) Kalamirides M, et al. 2008. Brain Pathol 18(1):62-70. (3) Zhu Y, et al. 2005. Development 132(24):5577-5588. (4) Morris ZS and McClatchey AI. 2009. Proc Nat Acad Sci 106(24):976-982.
			2005	
NF050014	Farassati	NF1	Demonstrated that Ras signaling level in MPNST cells determines susceptibility to treatment with oncolytic G207 virus.	(1) Farassati F, et al. 2008. Am J Pathol 173(6):1861-1872.
NF050028	Gutmann	NF1	Developed a non-invasive technique to detect optic glioma in mouse model of NF1.	(1) Banerjee D, et al. 2007. Neuroimage 35:1434-1437. (2) Hegedus B, et al. 2009. J Neuropathol Exp Neurol 68(5):542-551.
NF050052	Silva	NF1	Discovered that a Ras/ERK-dependent increase in GABA release may underlie learning deficits in NF1.	(1) Cui Y, et al. 2008. Cell 135(3):549-560.
NF050083	Belzberg	NF1	Developed the TNT model for neuroma pain and hyperalgesia.	(1) Dorsi M, et al. 2008. Pain 134:320-334.
NF050130	Weber	NF1	Identified NPM as a mediator of NF1 phenotypes and demonstrated that rapamycin effectively reduces NPM expression.	(1) Sandsmark DK, et al. 2007. Cancer Res 67(10):4790-4799.
NF050145	Mautner	NF1	Demonstrated effectiveness of Gleevec (imatinib mesylate) at treating plexiform neurofibromas in an animal model.	(1) Demestre M, et al. 2010. Science 98(1):11-19.
NF050171	Zhu	NF1	Provided evidence that mutations in NF1 may be responsible for learning deficits by impairing synaptic plasticity.	(1) Stornetta RL, et al. 2011. Neuroscientist 17:54-78.

Neurofibromatosis Research Program Accomplishments
CDMRP Public Affairs: 301-619-7071

Log Number	Principal Investigator	Type	Accomplishment	Relevant Publications
			2005	
NF050009	Ye	NF2	Provided evidence that Akt regulates merlin.	(1) Tang X, et al. 2007. Nat Cell Biol 9:1199-1207. (2) Okada M, et al. 2009. Cancer Res 69(9):4043-4051.
NF050193	Hansen	NF2	Demonstrated that the ErbB2 signaling pathway is essential for vestibular schwannoma growth.	(1) Brown KD, et al. 2008. Otol Neurotol 29(1):79-85. (2) Clark JJ, et al. 2008. Otol Neurotol 29(6):846-853. (3) Cioff JA, et al. 2010. Otol Neurotol 31(9):1455-1462.
NF050137	Perrimon	NF1/2	Developed technology to quantify phenotypic cell profiles facilitating screening for modifiers of NF1 and NF2 phenotypes.	(1) Bakal C, et al. 2007. Science 316(5832):1753-1756.
NF050153	Korf	NF1/2	Established the NF Clinical Trials Consortium.	
			2006	
NF060016	Korf	NF1	NF Clinical Trials Consortium began work on clinical trials for treatments of NF1.	
			2007	
NF073112	Yang	NF1	Generated a mouse model to study the mechanisms underlying NF1 skeletal manifestations.	(1) Xiaohua W, et al. 2011. PLoS One 6(9):e24917.
NF073094	Bretscher	NF2	Identified the structural conformation of normal and mutant merlin.	(1) Sher I, et al. 2012. Dev Cell 22(4):703-705.
			2008	
NF080045	Pumiglia	NF1	Demonstrated that alterations in NF1-deficient endothelial cells are dependent on Ras signaling.	(1) Bajaj A, et al. 2012. PLoS One 7(11):e49222.
NF080052	Ratner	NF1	Provided evidence supporting clinical trials of MEK inhibitors for NF1 MPNSTs.	(1) Jessen WJ, et al. 2013. J Clin Invest 123(1):340-347.
			2011	
NF110052	Korf	NF1/2	NF Clinical Trials Consortium expanded to include NF2 and schwannomatosis.	