Neurofibromatosis Research Program

Decreasing the Clinical Impact of Neurofibromatosis
HISTORY OF THE CDMRP

The Office of the Congressionally Directed Medical Research Programs (CDMRP) was created in 1992 from a powerful grassroots effort led by the breast cancer advocacy community that resulted in a congressional appropriation of funds for breast cancer research. This initiated a unique partnership among the public, Congress, and the military. The success in managing the initial congressional appropriations in breast cancer research, combined with additional advocacy movements and the need for focused biomedical research catapulted the CDMRP into a global funding organization for cancer, military medical, and other disease-specific research. The CDMRP has grown to encompass multiple targeted programs and has received over $8 billion in appropriations from its inception through fiscal year 2014 (FY14). Funds for the CDMRP are added to the Department of Defense (DoD) budget in which support for individual programs, such as the Neurofibromatosis Research Program (NFRP), is allocated via specific guidance from Congress.

APPLICATION REVIEW PROCESS

The CDMRP uses a two-tier review process for application evaluation with both steps involving dynamic interaction between scientists and clinicians—subject matter experts—and consumers. The first tier of evaluation is a scientific peer review of applications measured against established criteria for determining scientific merit. The second tier is a programmatic review, conducted by the Integration Panel (IP), which compares applications to each other and makes funding recommendations based on scientific merit, portfolio composition, and relevance to program goals.

CONSUMER ADVOCACY PARTICIPATION

A unique aspect of the CDMRP is the active participation of consumer advocates or patient representatives throughout the program’s annual cycle. Individuals with Neurofibromatosis (NF) (encompassing Neurofibromatosis Type 1 [NF1], NF2, and Schwannomatosis) and their family members have an equal voice in the research administration process of setting the NFRP’s vision, reviewing applications, and making final funding recommendations. From the unique perspective gained through personal experience, consumers bring a sense of urgency and focus to each part of the program cycle. Consumers evaluate the impact of the research to individuals with NF, as well as the needs of their family members, caregivers, and clinicians who treat them.
Neurofibromatosis
Research Program

NF is a group of three genetically distinct disorders that cause tumors to grow in the nervous system and also produces other abnormalities in the skin and bones. The tumors begin in the supporting cells that make up the nerve and the myelin sheath, and the type of tumor that develops depends on the type of supporting cells involved. There are three types of NF: NF1, NF2, and Schwannomatosis. An estimated 100,000 Americans have NF disorder, which occurs in both sexes and in all races and ethnic groups.

HISTORY OF THE NFRP
The NFRP was first funded in FY96 when the efforts of NF advocates led to a congressional appropriation of $8 million (M). Since that time, $272.85M has been appropriated to the program, including $15M in FY14.

FY96–FY14 Appropriations

FY96–FY12 NFRP Portfolio

NFRP has funded 292 basic, clinical, population-based, and resources research projects.

* Includes the FY06 and FY11 Neurofibromatosis Clinical Trials Consortium Awards with funding for both infrastructure and research.
**NF1**

**NF1**, also known as von Recklinghausen NF or peripheral NF, is the most common subtype of NF, affecting **1 in 3,000-4,000** people and results from a mutation in the **neurofibromin gene**. Although many affected individuals inherit the disorder, between 30% and 50% of new cases result from a spontaneous genetic mutation of unknown cause.

*“Having a child diagnosed with a rare and serious condition, such as NF, is challenging, to say the least. Learning more about NF and being an active member of the NF community gives me hope that effective treatments and an ultimate cure will be found for my child and the many thousands who live with NF.”*  

*Lori Ryan, Consumer Advocate Peer Reviewer*
Clinical Manifestations

Learning Deficits/Cognitive Disorders
- Attention Deficit Hyperactivity Disorder (ADHD)
- Speech and language delays
- Motor deficits
- Spatial deficits
- Asperger’s syndrome

Nervous System Disorders
- Neurofibromas
- Epilepsy
- Headaches

Visual Impairments
- Lisch nodules on the iris
- Retinal hamartomas
- Optic gliomas

Malignancies
- Malignant peripheral nerve sheath tumors (MPNSTs)
- Pheochromocytoma
- Chronic myeloid leukemia
- Brain tumors

Vascular Disease
- Dysplasia of blood vessels
- Hypertension

Skin Conditions
- Café-au-lait spots
- Dermal neurofibroma

Musculoskeletal Disorders
- Focal scoliosis and/or kyphosis of the spine
- Sphenoid bone dysplasia
- Congenital hydrocephalus

Malignancies
- Malignant peripheral nerve sheath tumors (MPNSTs)
- Pheochromocytoma
- Chronic myeloid leukemia
- Brain tumors

Vascular Disease
- Dysplasia of blood vessels
- Hypertension

Skin Conditions
- Café-au-lait spots
- Dermal neurofibroma

Musculoskeletal Disorders
- Focal scoliosis and/or kyphosis of the spine
- Sphenoid bone dysplasia
- Congenital hydrocephalus
Preclinical Murine Model for Fracture Healing in NF1
Feng-Chun Yang, M.D., Ph.D., Indiana University

Mutations in the NF1 tumor suppressor gene cause NF1, a common genetic disorder. Individuals with NF1 are afflicted with a range of malignant and nonmalignant manifestations and have significant risk for both generalized and focal skeletal abnormalities including osteoporosis, dystrophic scoliosis, increased fracture rates, and failure of bone fractures to heal properly.

Dr. Feng-Chun Yang of Indiana University has been the recipient of three separate NFRP awards to investigate the molecular mechanisms of bone abnormalities in NF1.

Dr. Yang first studied the biochemical and molecular mechanism underlying the pathological increase in de novo cytokine production in mouse Nf1+/- mast cells and human NF1 mast cells, and she evaluated whether mast cells from NF1 patients and mouse models have similar biological functions and cytokine secretion profiles. She found that murine Nf1 +/- mast cells secreted elevated levels of TGF-ß, VEGF, and PDGF, leading to the gain in fibroblast, endothelial cell, and Schwann cell biological functions. Dr. Yang also established that this gain in function is dependent on the Ras/PI3-K cell signaling pathway. In addition, she found that mast cells from NF1 patients have similar characteristics to those seen in the murine Nf1+/- mast cells, indicating that the biology of immune cells are comparable at certain levels between the human and murine system.

With additional funding from NFRP to investigate the role of Nf1 in the skeletal pathogenesis, Dr. Yang and her research team generated a conditional murine model in which one Nf1 allele was deleted from all tissues, and the remaining allele was deleted only in osteoblasts. These mice showed increased development and activity of osteoclasts (cells involved in bone resorption) and decreased osteoblasts (cells involved in bone formation), which resulted in severe impairment of fracture healing in this mouse model. Interestingly, administration of the MEK inhibitor PD98059 significantly improved the fracture healing process, indicating that targeting the MAPK signaling pathways may improve bone formation and prevent bone resorption in NF1.

Dr. Yang next sought to determine whether targeting the TGF-ß and MAPK pathway restores osteoclast functions, increases osteoblast differentiation, and thus enhances fracture healing. She utilized the conditional mouse model mentioned above and found significantly increased TGF-ß1 serum levels, which were also elevated in serum of a cohort of NF1 patients. Further, she was able to demonstrate that inhibition of the TGF-ß signaling with the pharmacologic inhibitor of the TGF-ß receptor I SD-208 rescued bone mass defects and prevented tibial fracture non-union in these mice. Overall, Dr. Yang’s studies demonstrate that dysregulated TGF-ß1 signaling is a primary factor underlying the pathogenesis of NF1-associated osteoporosis and non-union fracture. Therefore, pharmacologic inhibitors of TGF-ß signaling may be a potential therapeutic approach in the treatment for NF1 osseous defects, which are refractory to currently available treatments.

With NFRP funding, Dr. Yang and her team have made significant progress in the field of NF1 research, which may lead to new therapeutic targets that will help alleviate some of the debilitating effects experienced by patients with NF1.

Publications:
MEK Inhibition Prevents Brain Abnormalities Associated with NF1

Yuan Zhu, Ph.D., Children’s National Medical Center

NF1 is a complex genetic disorder characterized by the development of tumors in the nervous system. Often, affected children may also display a range of symptoms including bone abnormalities, larger-than-normal brain and head size, and accompanying learning disabilities. Clinical studies have shown that siblings with the same NF1 germline mutation may have dramatically different symptoms of the disease, indicating that NF1 disease severity depends on other genetic and/or epigenetic factors. Dr. Yuan Zhu had previously used sophisticated genetic manipulations in mice to inactivate the Nf1 gene in neural stem cells during embryonic development, and he discovered that mice with inactivation of both copies of the Nf1 gene had enlarged brains soon after birth due to a dramatic increase in the number of glial cells in the corpus callosum, similar to the brain abnormalities observed in some human NF1 patients with severe learning deficits. With funding from an FY10 Investigator-Initiated Focused Research Award, Dr. Zhu used these mutant mice to perform preclinical studies using drugs currently in clinical trials for treating cancer.

To identify the molecular pathways that contribute to this brain abnormality defect in these mice, Dr. Zhu used immunohistochemical staining techniques to detect activation of intracellular signaling pathways associated with Nf1 in the mouse brain. He found that the ERK signaling pathway was activated in brain cells from neonatal and adult Nf1 mutant mice with enlarged brains, whereas other signaling pathways commonly activated in Nf1 tumors were not. These results suggest that drugs targeting the ERK signaling pathway might be useful as a treatment to prevent the brain abnormalities seen in these mice. Based on these findings, Dr. Zhu treated newborn Nf1 mutant mice with the MEK/ERK inhibitor PD0325901 for 18 to 21 days, and he found that it completely prevented the brain enlargement observed in these mutant mice. This study demonstrates that deregulated ERK signaling is critical for the development of some of the brain abnormalities associated with Nf1 gene inactivation; it identifies a potential therapeutic agent (PD0325901) and highlights a window of opportunity for treating children with NF1-associated brain abnormalities.

Publication:
NF2, also known as Bilateral Acoustic NF (BAN), is a rare disorder affecting about 1 in 25,000 people and is caused by mutations in the Merlin gene. Approximately 50% of affected people inherit the disorder, while in others it is caused by a spontaneous genetic mutation of unknown cause.

Schwannomatosis is a much rarer disorder affecting about 1 in 40,000 people. Inherited forms of the disorder account for only 15% of all cases. Researchers have identified a mutation of the SMARCB1/INI1 gene that is associated with the familial form of the disease, but they do not fully understand what causes the intense pain that characterizes the disorder.

The NFRP has funded:

- 69 NF2 projects
- 9 Schwannomatosis projects
- 2 NF2/Schwannomatosis projects
- 11 NF1/NF2 projects

Together, these awards account for 31% of the total number of projects funded by the NFRP.

"I was diagnosed with NF2 at the age of 9 years old, subsequent to my father's diagnosis of the same condition in his early 40’s. The disease has affected me, and my family, in many ways – financially, emotionally, physically, and tragically. I highly recommend that individuals afflicted with this disease get involved and become consumer advocates. I cannot begin to describe how important it is for an individual suffering from this disease to become actively involved—and there is no better place than this organization to start."

Frank Buono,
Consumer Advocate Peer Reviewer
Clinical Manifestations

NF2
Non-malignant Tumors
• Vestibular schwannomas
• Spinal cord tumors
Malignant Brain Tumors
Headaches
Visual Defects
Hearing Loss

Schwannomatosis
Non-malignant Tumors
• Schwannomas (non-vestibular)
Headaches
Neurological Symptoms
• Numbness
• Tingling
• Weakness in fingers/toes
Chronic Pain

“After working with NF patients and families for many years, it was a very meaningful experience for me to be part of the peer review panel; it gave me a clear overview of the goals and objectives of the program. The mix of clinicians and basic science researchers produces a remarkable opportunity to learn and to see the disease from two different perspectives. The NFRP is a unique program that combines expertise in the field – employing an exceptional selection of NF experts – with the views of consumer advocates. This is an uncommon pairing; however, it offers a rare opportunity to provide real solutions to patients with conditions like NF. Having consumer advocates in the peer review process is a vital element of the program. It is important for the researchers to understand patients’ needs. In the end, that is what it is all about.”

Maria T. Acosta, M.D.,
George Washington University/Children’s National Medical Center,
Scientific Peer Reviewer
Characterization of an NF2 Model that Develops Intracranial Vestibular Schwannomas and Meningiomas Associated with Hearing Loss

D. Wade Clapp, M.D., Indiana University

The primary manifestation of NF2 is the development of vestibular schwannomas – non-malignant tumors that form in the region of the auditory vestibular nerve, which transmits sensory information from the inner ear to the brain. As such, most NF2 patients will eventually experience complete hearing loss due to the growth of these tumors. Existing mouse models of NF2 develop tumors in peripheral nerves and spine, providing a valuable resource for understanding disease pathogenesis and developing more effective therapeutic drugs. However, these animal models do not fully mirror the hearing loss and vestibular dysfunction commonly found in patients with NF2. Dr. Wade Clapp, recipient of an FY11 Exploration–Hypothesis Development Award through the DoD NFRP, has developed an NF2 mouse model that appears to form not only intracranial vestibular schwannomas and meningiomas, the most common brain tumors found in individuals with NF2, but also develops progressive hearing loss as well.

Dr. Clapp and his collaborators performed auditory brainstem response testing to determine the timeline of hearing impairment in these mice. They have shown that although these mice have no structural defects in the inner ear (cochlea), they develop hearing loss beginning at 8 months of age, and this hearing loss grows more severe by 10 months of age; it is functionally equivalent to being unable to hear a normal conversation. This timeline is in agreement with histological analysis of brains from these mice, showing that by 8 months, 100% of the mice develop vestibular schwannomas associated with the proximal spinal nerve and dorsal root ganglion responsible for transmitting nerve impulses for both balance and hearing. Altogether, Dr. Clapp’s data suggest that this NF2 animal model will be a valuable tool with which to study disease pathogenesis and novel drugs targeting molecular pathways thought to be important to tumor development in NF2 and associated hearing loss.

“My experience participating in the NFRP review have been eye opening and very positive. The concept of including a patient advocate in the actual review is fantastic and an example for other funding agencies. It helps the scientists better appreciate the most pressing clinical concerns and informs the patient advocates about the latest developments in the research arena. This benefits all parties and results in prioritizing the most translational and timely projects.”

Jacob Raber, Ph.D., Oregon Health & Sciences University, Scientific Peer Reviewer
Mouse Model of Schwannomatosis-Related Neuropathic Pain

Jeremy Vitte, Ph.D., House Research Institute

Schwannomatosis patients develop extremely painful spinal, peripheral, and cranial-nerve Schwann cell tumors (schwannomas) and frequently suffer from additional neurological symptoms including numbness and weakness in the extremities. Although the mechanism of Schwann cell tumor development is not fully understood, recent studies suggest that mutation of the tumor suppressor gene Snf5/Ini1/SMARCB1 may be involved in familial schwannomatosis. Recent data also suggests that inactivation of the NF2 gene may also play a role in SMARCB1-initiated schwannoma development.

Dr. Jeremy Vitte, with funding from an FY09 NFRP Postdoctoral Traineeship Award, successfully developed a preclinical animal model to better understand the role of Snf5 in Schwann cell tumor development and schwannomatosis-related neurological pain. Interestingly, preliminary data suggests that inactivation of both Nf2 and Snf5 in the novel preclinical model results in the development of nerve lesions. Dr. Vitte has also developed a collaboration with investigators at the University of California, Los Angeles, to evaluate the role of Snf5 in schwannomatosis neuropathic pain.

“The NFRP funds the most significant basic, translational, and clinical research specifically targeting neurofibromatoses (NF1, NF2, and Schwannomatosis) of any organization in North America. NFRP-funded research has contributed to important advances in the understanding of the molecular bases of various aspects of NF and to important therapeutic efforts now in progress to improve the survival and quality of life of NF patients. I am pleased that in my long association with the NFRP as a scientific peer reviewer, then as a member of the Integration Panel and now as Chair of the Integration Panel, I have been able to contribute in small ways in assisting the NFRP in choosing and supporting the most scientifically meritorious studies for funding by the NFRP, and am confident that the IP will help keep the NFRP on a trajectory to further improve knowledge and treatment for patients with NF.”

Douglas Miller M.D., Ph.D., University of Missouri School of Medicine, IP Chair
The Neurofibromatosis Clinical Trials Consortium (NFCTC, http://www.uab.edu/nfconsortium) was established by the DoD NFRP to develop and perform clinical trials for the treatment of NF complications in children and adults. The Consortium is composed of thirteen clinical sites, five collaborating sites, and an Operations Center at the University of Alabama at Birmingham under the direction of Dr. Bruce Korf. The purpose of the Operations Center is to provide administrative, data management, and statistical support to the NFCTC. Each of the clinical and collaborating sites has expertise in the treatment and management of NF and an established patient population available for clinical trials.
**STOPN: Sirolimus for the Treatment of NF1-Related Plexiform Neurofibromas**

STOPN is a Phase II clinical trial to evaluate the mTOR inhibitor Sirolimus in the treatment of plexiform neurofibromas in children and adults with NF1. The goals of this trial are to (1) evaluate the feasibility and toxicity of chronic Sirolimus administration and (2) characterize the active pharmacokinetic profile of Sirolimus when administered to this patient population.  

*ClinicalTrials.gov Identifier: NCT00634270*

**STARS: Lovastatin for the Treatment of Learning Disabilities in Children with NF1**

STARS is a placebo-controlled, double-blind Phase II clinical trial to evaluate the effectiveness of Lovastatin™ in the treatment of learning disabilities in children with NF1. The goals of this study are to (1) determine whether Lovastatin™ significantly improves visual spatial learning and/or sustained attention in children with NF1, (2) evaluate the effect of Lovastatin™ on measures of executive function, behavior, and quality of life in children with NF1 and cognitive deficits, and (3) evaluate the toxicity and tolerability of Lovastatin™ in children with NF1 and cognitive deficits.  

*ClinicalTrials.gov Identifier: NCT00853580*

**RAD001: RAD001 for Children with NF1 and Chemotherapy-Refractory Radiographic Progressive Low-Grade Gliomas**

This is a single-arm Phase II trial to evaluate the effectiveness of RAD001 (everolimus) in the treatment of pediatric patients with NF1 and low-grade gliomas (brain tumors and optic gliomas) that have not responded to standard therapies. In addition to evaluating the clinical response to RAD001, the safety of this drug will be evaluated in this patient population.  

*ClinicalTrials.gov Identifier: NCT01158651*

**MPNST: RAD001 in Combination with Bevacizumab for Patients with Sporadic and NF1-Related Refractory MPNST**

MPNST is a Phase II clinical trial of RAD001 (everolimus) in combination with bevacizumab (Avastin) for patients with sporadic and NF1-related refractory MPNST. The primary goals of this trial are to evaluate the clinical benefit of treatment of chemotherapy refractory MPNST with RAD001 in combination with bevacizumab and assess the toxicity and safety of this drug combination. This study is being performed in collaboration with the Sarcoma Alliance for Research through Collaboration.  

*ClinicalTrials.gov Identifier: NCT01661283*

**Bevacizumab for NF2-Related Progressive Vestibular Schwannomas**

This is an open-label, Phase II clinical trial to evaluate bevacizumab (Avastin) in children and young adults with NF2 and progressive vestibular schwannomas that are poor candidates for standard treatment with surgery or radiation. The primary objective of this study is to determine the hearing response rate at 24 weeks after beginning treatment with bevacizumab for symptomatic vestibular schwannomas in children and young adults with NF2.  

*ClinicalTrials.gov Identifier: NCT01767792*

**Cabozantinib (XL184) for NF1-Related Plexiform Neurofibromas**

This Phase II clinical trial will evaluate the response rate of adolescents and adults with NF1 and plexiform neurofibromas treated with Cabozantinib (XL184).  

*ClinicalTrials.gov Identifier: NCT02101736*

**PD-0325901 for NF1-Related Plexiform Neurofibromas**

This Phase II clinical trial will evaluate the MEK inhibitor PD-0325901 for the treatment of NF1-related morbid plexiform neurofibromas in adolescents and adults.  

*ClinicalTrials.gov Identifier: NCT02096471*
Sharon and Elana Loftspring – A Mother-Daughter Team Against NF

I recently added a few pages to my daughter’s scrapbook using paper designed with lemons. The phrase “turning lemons into lemonade” fits her perfectly. Elana has NF1. She was diagnosed when she was five, and the diagnosis has had a profound effect on both her life and mine.

I have been active in the NF Network, formerly Nf, Inc., on a local level and a national level for over 10 years. A representative from the organization greeted me at our first visit to an NF clinic, and provided resources to help me educate myself about the condition. Once I became involved, I was introduced to a network of parents, like myself, who were searching for answers, advocating for their children, and seeking support. Many of those parents have become dear friends over the years—my “lemonade.”

It was through that organization that I first learned about the NFRP. I joined a group of NF, Inc. individuals who visit Capitol Hill every year to advocate for research funding for NF. I distinctly remember getting a crash course on the DoD’s CDMRP and being so impressed by their implementation. The following year, I served as a consumer reviewer of the grant proposals submitted for NF research and have continued to do so since that time. The experience has been invaluable to me—not only is the process informative about the happenings in the medical research arena, but it is rewarding to know that my opinion is valued.

In 2009, Elana’s NF specialist discovered a brain tumor during a routine MRI. I immediately connected with my NF contacts and was led to the “right” specialists for our family. Her surgery was a success! Although it was traumatic for Elana in many respects, she managed to turn it into something positive. She began to make personalized care packages for other children affected by NF. Here’s how Elana describes the project in her own words:

“I knew what it was like to feel alone, and it felt awful! So I put a notice on the NF Network website and received emails from parents explaining their child’s troubles. Then I would respond by asking what the child liked to do, and would use that information to pick out things for the package. I would also include a letter from myself explaining that I, too, had NF, and that they were not alone. I ended up sending roughly 100 packages across the country.”

Last summer, Elana connected again with kids who have NF by attending Camp New Friends in Virginia. She loved it! Elana describes her camp experience this way: “I met nearly 65 other people with NF. I found what I had always wanted – people like me. Although our symptoms were unique, we were all the same. I understood exactly what the campers were feeling when they talked about their MRIs and medical tests, and they understood me. It felt great!”

Our connection to the NFRP came full circle this year when Elana came with me to advocate for continued funding of NF research. We were able to hear about the great strides that scientists are making in the field of NF research, and even clinical trials, and how the NFRP is keeping up the momentum. Elana used her voice to tell her story in the hopes that these programs will continue.

Elana’s diagnosis has opened our eyes to other families affected by NF, to a dedicated scientific community that is committed to working toward finding a cure, and to connections with young people who remind Elana that she is not alone in this fight. As I said, Elana has truly transformed lemons into lemonade!
Andrés Lessing – A Long-time Neurofibromatosis Advocate

Andrés Lessing was diagnosed with NF1 more than 33 years ago, before the gene responsible for the disease had been identified. Although his illness has been mild for most of his life, 6 years ago he received a more threatening diagnosis: a malignant peripheral nerve sheath tumor had been discovered. Four years have passed since his last recurrence.

Andrés has been active in helping people with NF since the late 1990s. He became involved with Neurofibromatosis Northeast, with the initial development of its website and serving as one of the organization’s first trustees. Along with his father, he helped organize a fundraising event – Bike Ride for NF, in Cape Cod – which not only raised money for Neurofibromatosis Northeast, but also provided a framework for bringing together people affected by NF.

Neurofibromatosis Northeast nominated Andrés to serve as an NFRP consumer peer reviewer, and he was invited to join the review panel. After the first meeting, he described the review experience as “amazing...to be part of the peer review process in selecting the best research to pursue. It was very rewarding to be at the same table as researchers and clinicians, and others affected by NF.” He has remarked that consumers and scientists alike were encouraged to express their opinions and ask questions. Andrés left the meeting convinced not only that his concerns had been heard but that the work the panel had accomplished would help to ensure that the limited funds available would go to the best projects.

An avid bicyclist and father of two children, Andrés observes, “Every year progress is made. I know this because I get daily updates from government-funded research and am able to participate in research studies myself. Knowing where we were 30 years ago, where we were 10 years ago, and where we are now, I know that we are headed in the right direction.” The need to continue research is critical, and this consumer’s fervent hope is that the government continues to recognize the urgency to fund NF research, which, as he points out, has not only led to increased knowledge of NF but of other diseases as well, including many forms of cancer.
Promoting research directed toward the understanding, diagnosis, and treatment of NF1, NF2, and Schwannomatosis to enhance the quality of life for persons with those diseases.

NFCTC

Nancy Ratner, Ph.D.
Children’s Hospital Medical Center

Maura Cosetti, M.D.
New York University School of Medicine

David Gutmann, M.D., Ph.D.
Washington University School of Medicine

For more information, visit
http://cdmrp.army.mil
or contact us at:
usarmy.detrick.medcom-cdmrp.mbx.cdmrp-public-affairs@mail.mil
(301) 619-7071