A GROWING CRISIS, A VISION OF HOPE
NBRI Co-Directors: Donna Ferriero, MD & David Rowitch, MD, PhD

Donna Ferriero, MD, chief of Pediatric Neurology and professor of Neurology at UCSF Children’s Hospital, is an internationally recognized expert in newborn brain dysfunction, including the care of babies and children with neurological disabilities. Ferriero’s research is focused on understanding mechanisms of brain injury in newborns, especially newborn stroke. A member of UCSF’s faculty since 1987, Ferriero earned her medical degree from UCSF and trained in Boston and at UCSF. She is a member of the Institute of Medicine.

“We must build sustained funding for this vital program so we can eliminate neurological infant brain problems and save those babies yet to be born from lifelong medical conditions.” — Donna Ferriero, MD,

David Rowitch, MD, PhD, is chief of Neonatology and professor of Pediatrics and Neurological Surgery at UCSF Children’s Hospital. Rowitch’s groundbreaking research has identified how neural stem cells are controlled during brain growth and repair. Trained at Harvard and educated at UCLA and Cambridge, Rowitch has received numerous research awards and is a Howard Hughes Medical Institute Investigator. He moved his laboratory from Harvard Medical School in 2006 to what is now named The Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research at UCSF to help found the NBRI.

“The baby brain already exhibits the ability to repair itself. By unleashing this potential, we intend to better understand and effectively treat neurological issues facing premature and term babies.” — David Rowitch, MD, PhD,
INTRODUCTION

Each year tens of thousands of premature infants develop moderate to severe brain abnormalities. As doctors save the lives of more and more premature infants, the number of newborns with abnormal brain function is increasing, yet no effective treatments exist. Nearly 50% of premature babies will develop abnormal brain functions, and 15% of these will have such severe disabilities that lifelong care will be required. Compounding this growing problem, funding for newborn brain research remains scarce.

Responding to this public health crisis, UCSF Children’s Hospital has established an ambitious program: the Newborn Brain Research Institute (NBRI). Concentrating world-class medical talent and applying promising research approaches, the NBRI is pioneering medical breakthroughs for newborns with neurological complications.

Our goal is to one day eliminate brain abnormalities in infants by unlocking the developing brain’s innate ability to protect and repair itself.

ESTABLISHMENT OF THE NBRI

Although UCSF already has a critical mass of basic researchers in the neurosciences, it lacks optimal integration of these resources to focus on the problem of newborn neurological injury. In response to rising rates of neurodevelopmental deficits in preterm infants (including cognitive/learning problems and severe cerebral palsy), UCSF established the NBRI in 2006.

The NBRI is promoting greater interactions amongst researchers within UCSF as well as inter-institutional collaborations. We have applied to become an NIH-funded “Intellectual and Developmental Disabilities Research Center (IDDRC),” which will provide resources for Core facilities to promote collaborative research.

In 2008, we opened the nation’s first “Neuro-Intensive Care nursery (NICN)” at UCSF. The NICN provides intensive neurological monitoring and comprises a unique interdisciplinary team of neonatologists, neurologists, nurses, nurse practitioners, developmental specialists and neuro-radiologists focused on infants with neurological complications. It will define state-of-the-art care and serve as a platform for clinical investigation into novel neuroprotective treatments for newborn neurological problems.
Fostering Goals of the NBRI through “Translational Research”

“Translational research” refers to an area of investigation that seeks to bridge the gap between our understanding of basic science and its clinical application. While we have made many remarkable advances in terms of our understanding of neural stem cell developmental biology, relatively little attention has been paid to applying messages from the basic sciences to better understanding newborn neurological injury as a means of developing new types of therapeutic options.

The NBRI fosters translational research, a multi-disciplinary effort that connects both basic scientists and clinical researchers integrated into the following thematic areas.

Basic Research

The NBRI brings together some of the world’s top neuroscientists to focus on problems in brain development that can lead to injury including cerebral palsy.

Some current examples of NBRI basic research studies are:

**Defining the “landscape” of the developing human brain.** NBRI scientists are collaborating to examine the human fetal and neonatal brain to define the nature of the developing stem cell niche. This information will then be used to establish the impact of various injuries (stroke, infection, prematurity, etc.) on neural stem cell populations in patients.
Understanding causes of Periventricular Leukomalacia (PVL). We have used novel markers of “oligodendrocytes” (the myelinating cells of the brain) to re-define the pathogenesis of PVL, a condition in premature infants that leads to cerebral palsy. We find that oligodendrocytes show impaired ability to differentiate and repair in PVL, an observation that is promoting new research directions.

A neurosphere: This is preparation that NBRI scientists use to study the potential of primitive stem cells in the brain and their ability to make other specialized cell types. Such cells may one day be the basis of cellular therapies.

Discovering novel neuro-protective mechanisms. NBRI researchers have recently identified the Sonic hedgehog pathway as protective against the harmful effects of glucocorticoids (steroids) in the neonatal brain and that the hormone erythropoietin (EPO) is protective in hypoxic neonatal brain injury. Such approaches may one day find their way into clinical use.

Clinical-Translational Research Infrastructure

The NBRI is supporting development of new research units designed to promote clinical and fundamental scientific advances.

The Neurointensive Care Nursery (NICN). We established the nation’s first Neurointensive Care Nursery at UCSF in 2008, with the generous support of private donors. The NICN offers specialized medical, nursing and imaging capabilities and has treated almost 100 patients in its first year of operation with clinical hypothermia (cooling therapy) for full term infants at risk for brain injury. The UCSF infant follow-up clinic provides detailed assessment of patients over time, physical and occupational therapy and ongoing family support. The NICN is raising the standards of clinical care for infants with neurological injury today and it will facilitate the “neuro-protective” clinical studies of tomorrow.

http://neonatology.ucsf.edu/nbri
**The HHMI Pediatric Brain Research Laboratory.** With generous support from the Howard Hughes Medical Institute (HHMI), we have established the Pediatric Brain Research Laboratory (PBRL) at UCSF. The PBRL tissue bank enables detailed investigation of the infant brain. This includes analysis of the genes and proteins that could provide vital clues about disease mechanism and susceptibility. The PBRL will support research at UCSF and the work of investigators around the world.

**Clinical Research**

UCSF is a leader in brain imaging research to diagnose injury. We lead a nationwide study to better repair neural tube defects, also called “spina bifida.” Please check our website (www.neonatology.ucsf.edu/nbri) for further information about the following clinical trials:

**MOMS Study.** This study will determine whether fetal closure of myelomeningocele (aka, spinal bifida or neural tube defects) is more effective than closure after birth. This study is funded by the National Institutes of Health (NIH).

**PREMIRI Study.** This study uses magnetic resonance imaging (MRI) to assess brain development in babies that are born prematurely. The study is funded by the NIH.

**BAMRI Study.** This study uses magnetic resonance imaging (MRI) to assess possible brain injury in babies that may have suffered from lack of oxygen or blood supply to the brain around the time of birth. This study is funded by the NIH.

![MRI images showing brain development in a premature baby: UCSF researchers use MRI images in groundbreaking ways to study structure, function and damage in the developing human brain.](image)

**HuCNS-SC™ in PMD Phase I Safety Study.** This FDA-approved study will assess the safety and tolerance of human neural progenitor transplants in patients with Pelizaeus-Merzbacher Disease, a rare disorder in which the brain profoundly lacks myelin, an insulating substance for nerve cells critical for their function. Funded by StemCells, Inc., a biotechnology company in Palo Alto, California.
NEW DIRECTIONS AND THE CHALLENGES AHEAD

The NBRI will foster further clinical-translational progress through three key efforts that will require grant and philanthropic support:

Intellectual and Developmental Disability Research Center (IDDRC) at UCSF. To better integrate investigators at UCSF to research critical problems affecting development of the newborn brain and brain injury, the NBRI is fostering an “Intellectual and Developmental Disorders Research Center (IDDRC).“ This application to the National Institute of Child Health and Development will support new and innovative scientific research units.

Junior Faculty Recruitment. It is essential to pave the way for the next generation of talented investigators committed to researching brain injury in infants and developing new modes of therapy. The NBRI will support hiring new faculty in UCSF basic and clinical departments.

“Building” the NBRI. Although the NBRI currently exists as a “virtual” institute, as we move forward we envisage that the NBRI will comprise a suite of laboratories and perhaps a free-standing building at UCSF to encourage synergy and interactions between investigators.

HOW TO HELP

To find out how you can help bring the Newborn Brain Research Institute’s vision to life and fund its vital research, please contact the UCSF Development Office at 415-476-4644.

Donations can be mailed to the UCSF Foundation, Box 0248, San Francisco, CA 94143-0248 (please note “NBRI” on your check) or online at https://makeagift.ucsf.edu/ and indicate “NBRI” in the additional instructions box.

Thank you for your interest in the NBRI.

http://neonatology.ucsf.edu/nbri