

# University of California, Davis

## Center for Children's Environmental Health

### *Environmental Factors in the Etiology of Autism*

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#### Overview

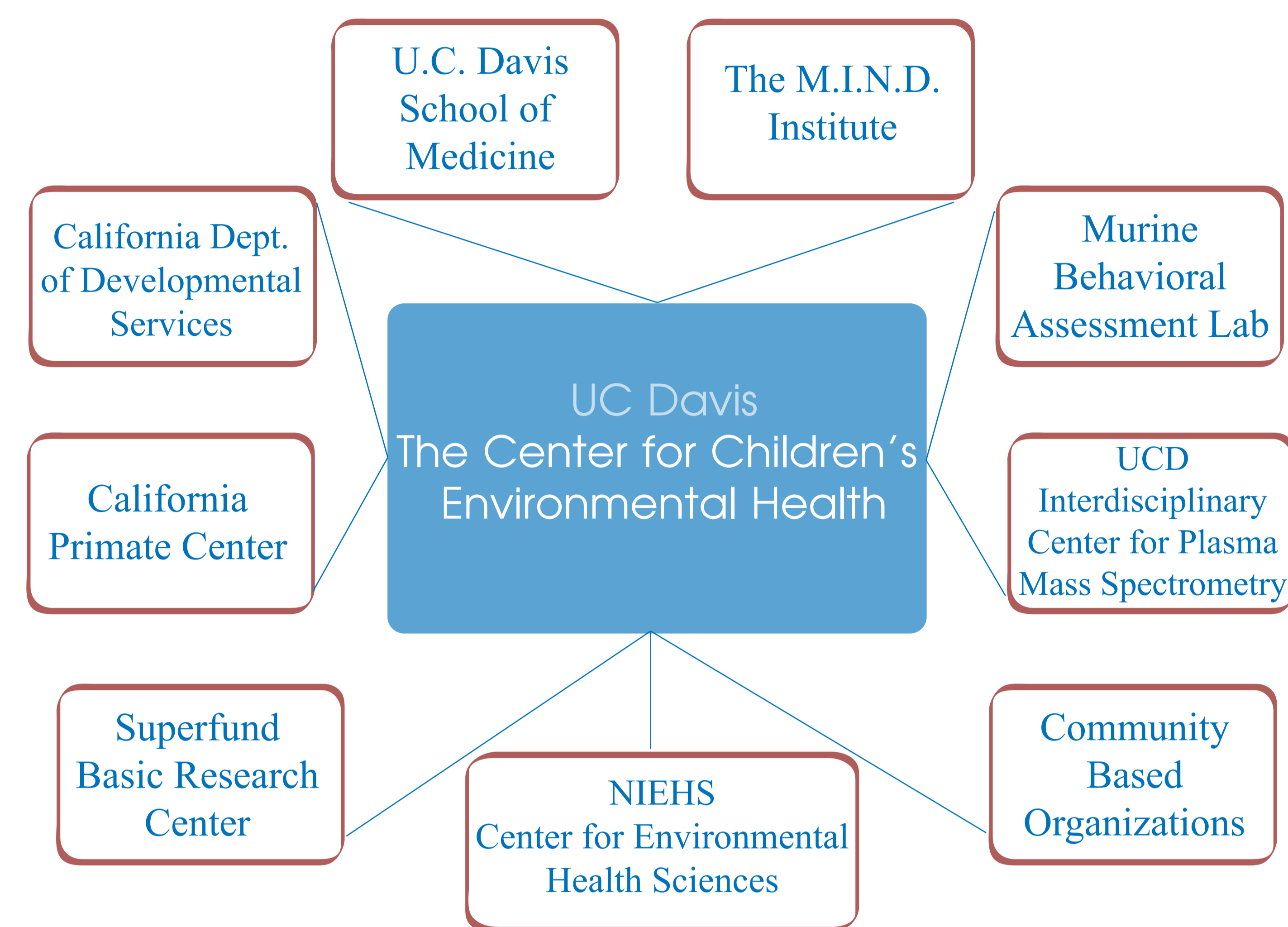
The primary focus of the U.C. Davis Center for Children's Environmental Health is to understand environmental risk factors contributing to the incidence and severity of childhood autism. Autism is a neurodevelopmental disorder defined by deficiencies of social reciprocity and communication, and by repetitive behavior (American Psychiatric Association, 2000).

Surveys in California have indicated an apparent 210% increase in the cases of profound autism in children diagnosed over the last 10 years. Recent estimates indicate the frequency of mild to severe autism may be as high as 1:150 (Lord et al 2000).

Clearly there is a critical need to understand how the interaction of susceptibility genes with exposure to environmental chemicals may increase the risk and severity of autism and to identify which combination of chemical exposures confer the greatest threat. To meet

the pressing need to define etiological risk factors in autism, we established a broadly based center of excellence that brings together a multidisciplinary team whose major focus is to identify the genetic and environmental factors that influence risk of childhood autism. Our ultimate goal is to understand common patterns of dysfunction in autism and elucidate mechanisms by which known neuroimmunotoxicants contribute to abnormal development of social behavior in children so that rational strategies for intervention and prevention can be undertaken.

The very essence of the Center at UC Davis is to facilitate scientific exchange among epidemiologists, pediatric neurologists, toxicologists, neurobiologists, immunologists and molecular biologists that have a common goal; gaining an understanding of the social deficits attributed to childhood autism so that prevention, treatment and cures can be offered.



#### Research Projects

**Research Project I – The CHARGE Study:** This is a case-control study that integrates procurement of exhaustive information about environmental exposure and tissue samples from a total of 2000 California children (700 autistic, 700 mentally retarded but nonautistic controls and 600 typically developing controls) and their immediate family. Biological samples collected in Project I are extensively characterized for xenobiotic, cellular and molecular biomarkers for autism.

**Research Project II - Animal Models of Autism:** Project II is conducting mouse studies to determine how early postnatal or perinatal exposure to known immunotoxicants and neurotoxicants in the presence and absence of immune challenge influences normal development of social behavior. In addition we have established a comprehensive ethogram for testing many aspects of social behavior in the rhesus monkey at the CA Regional Primate Center. These measures provide the closest detail of modeling how early maternal viral challenges influence subtle aspects of social behavior and if the exposure influences susceptibility to postnatal thimerosal.

**Research Project III - Cellular and Molecular Mechanisms of Autism:** The elucidation of molecular and cellular mechanisms underlying abnormal development of brain regions conferring important determinants of social behavior is the charge of Project III. Detailed studies on hypotheses related to the underlying mechanisms conferring susceptibility to the immunotoxic and neurotoxic agents are being undertaken.

collected from Research Projects I and II, and tissue culture experiments performed in Project III are being analyzed for markers of cellular activation, including cytokine, neurotrophic peptides and autoantibody production.

**Facility Core III - Molecular Biomarkers Core:** The primary goal of the Molecular Biomarkers Core is to identify patterns of altered gene expression that form a significant association with autism in human populations, or which are coupled to specific environmental factors in animal models. The Core is designing and printing global and focused microarrays for molecular analysis of samples generated by Center Investigators.

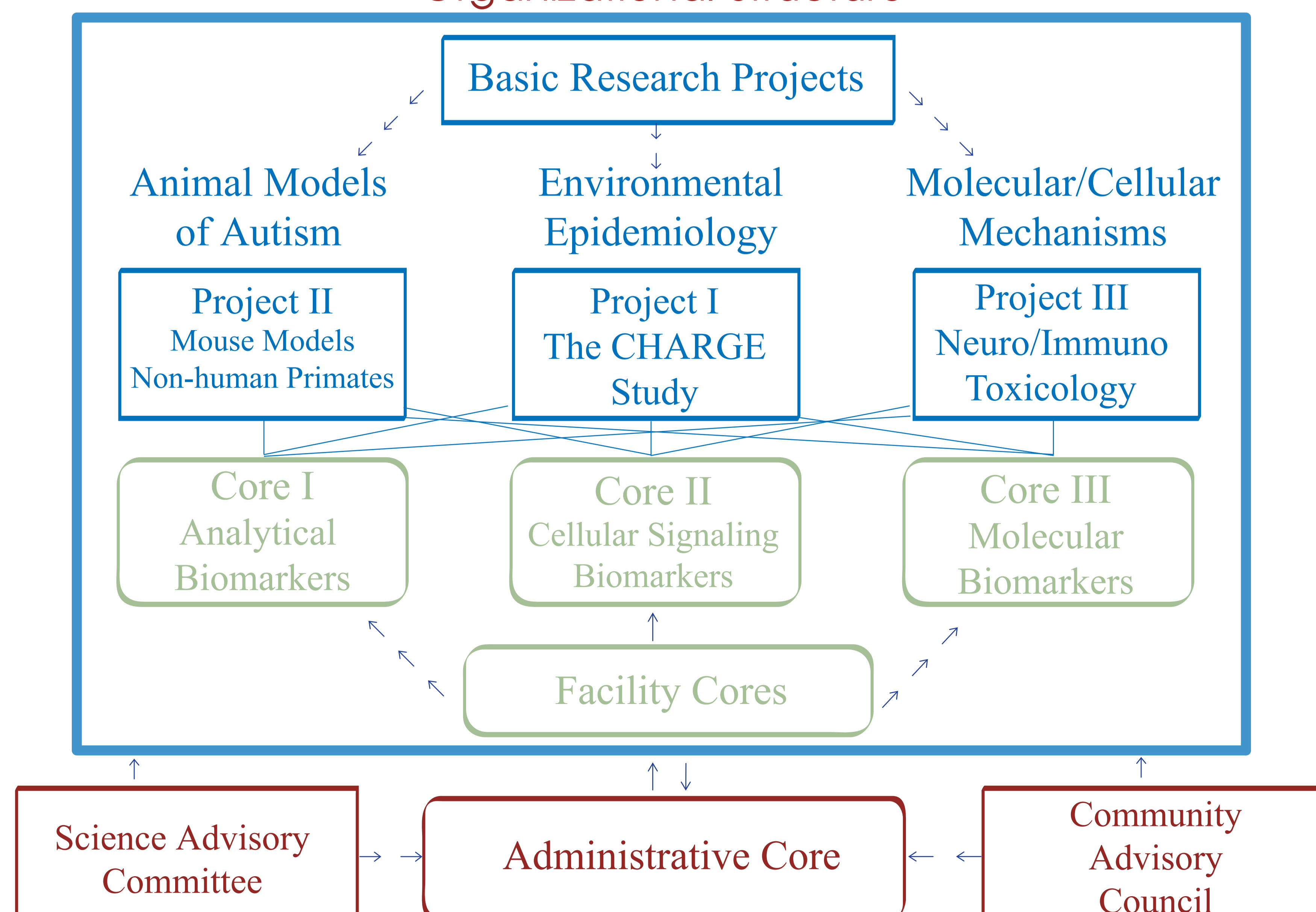
**Administrative Core:** The Administrative Core coordinates interactions among Center participants by organizing monthly investigator meetings and provides coordination and support for the Community Advisory Council and Science Advisory Committee. The core also serves as the liaison for Center interactions with extramural partners including, subcontractors, community groups, as well as the various Institutional Review Boards. The core also participates in and coordinates outreach and education activities.

#### Cores

**Facility Core I - Analytical Biomarkers (Xenobiotics):** The Analytical Core provides general analytical support to the program investigators including either running samples for scientists in the project, providing training to scientists on the capabilities and the uses of the core instrumentation or consulting on method development. The Core philosophy is to have a variety of analytical methods to look at xenobiotics in tissues as well as natural biomarkers. One of the major goals of this core is to provide support in metabolomics.

**Facility Core II - Cell Activation/Signaling:** Core II provides a diverse array of serologic and cellular test parameters and expertise that are available for use to all center scientists. Specifically samples

#### UC Davis Center for Children's Environmental Health Organizational Structure



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