Hello, this is Kevin O'Donovan, and I'd like to welcome you to the National Institute of Environmental Health Sciences Superfund Research Program monthly Research Brief podcast.

This month, we're discussing how cell-based models reveal differences in how polycyclic aromatic hydrocarbon mixtures affect neurodevelopment.

The Research Brief, Number 267, was released on March 1, 2017, and was written by SRP contractor Sara Amolegbe in conjunction with SRP-supported researcher Theodore Slotkin.

Exposure to a mixture of polycyclic aromatic hydrocarbons (or PAHs) may produce different neurodevelopmental effects from those of exposure to individual PAHs, and the developing brain may be sensitive to these contaminants over a wide window of development, according to a Duke University Superfund Research Program Center study.

Researchers identified direct effects of an environmentally relevant PAH mixture and a single PAH, benzo[a]pyrene (or BaP), at two different points in neurodevelopment, reinforcing the need to consider mixtures rather than single compounds in exposure studies. The study also provided mechanistic evidence for associations between developmental PAH exposures and behavioral deficits that have been previously observed in children and animals.

Researchers led by Theodore Slotkin evaluated neurodevelopmental effects of BaP and a PAH mixture obtained from the Elizabeth River Superfund site. They used two cell-based models that assess distinct transitions during neurodevelopment to determine the specific changes within cells that may contribute to developmental effects.

The first cell-based model, which uses pheochromocytoma (PC12) cells, has been used in thousands of studies to evaluate neurodevelopmental neurotoxicants. PC12 cells can be made to develop into neurons, the basic working unit of the brain. Neurons are the cells that transmit the information to enable learning, memory, emotion, and all of the other functions we associate with a working brain. Because PC12 cells undergo the essential processes that make a cell into a neuron, this model can be used to assess how exposure to chemicals affects neuron development. The researchers found that BaP impaired the transition into neurons, resulting in a higher number of smaller cells with deficits in neuronal features, including impaired neuronal projections and reduced differentiation into specific neurotransmitter types. On the other hand, the environmental PAH mixture did far less damage and only caused modest changes in cell numbers and size and no impairment of neuronal features.

The second cell-based model, which used embryonic neural stem cells (or NSCs), considers an earlier point in neurodevelopment at which NSCs choose to become neurons or glia. Glia support and protect neurons and provide guidance for the migration of neurons to their proper location in the developing brain. In contrast to the PC12 cell model, the NSCs were much more sensitive to exposure to the environmental PAH mixture than to BaP. The environmental mixture enhanced the formation of neurons, resulting in a profound drop in the glia-to-neuron ratio, which can affect brain homeostasis and function.

In the study models, BaP targeted the later point in neurodevelopment, modeled by PC12 cells, much more than the earlier point, modeled by NSCs. But for the environmental PAH mixture, the researchers found the opposite, with greater sensitivity to the earlier point in neurodevelopment. The findings provide mechanistic information on how early-life PAH exposure can lead to neurodevelopmental and behavioral deficits due to impairment at multiple endpoints.

According to the authors, the study findings show that a complex PAH mixture can produce effects that differ in direction and magnitude from those of a single PAH like BaP. These differences may be a result of interactions among mixture components and may indicate potential health effects over a wider window of development, ranging from the earliest decision points when neurons and glia are formed through their later stages of development into specialized structures. Because sensitivity to different PAHs may occur during various developmental stages, the authors suggest that vulnerability to PAH exposure likely extends throughout fetal brain development and into early childhood.

If you'd like to learn more about this research, visit the Superfund Research Program website at www.niehs.nih.gov/srp. From there, click on "Who We Fund" and follow the links to the Duke University research summary. If you have any questions or comments about this month's podcast or if you have ideas for future podcasts, contact Maureen Avakian at avakian@niehs.nih.gov.

Join us next month as we discuss more exciting research and technology developments from the Superfund Research Program.