HPV Vaccine: A Tool for Cancer Prevention

I t is in this modern age it is likely that nearly every day we are exposed to chemicals that may have the potential to cause cancer. From hydropower in diesel exhaust to nitrosamines in beer, low level carcinogen exposure is essentially unavoidable. While specific exposure can lead to cancer, the human body also has evolved a variety of mechanisms to adapt to these environmental threats.

Christopher Bradford, PhD, director of the Molecular and Environmental Toxicology Center at UW-Madison and UW Carbone Cancer Center (UWCCC) member, is a toxicologist leading a team focused on understanding how we adapt to environmental insult while trying to answer the complex questions that surround exposure-risk calculations. “There are dozens of environmental stimuli that we encounter every day,” he says, “and it’s really hard to pinpoint what level of impact any of them will have on a person’s health.”

Bradford, professor of oncology at the UW School of Medicine and Public Health, has a lab at the Microbiology Laboratory for Cancer Research. There Bradford and his colleagues work to discover the causes of human cancer, how to treat it and how to prevent it.

The start of Bradford’s research journey began in the 1980s when he noted that some of our most toxic synthetic chemicals, such as dioxins, and highly touted antioxidants from plant foods showed evidence to work through the same receptor, the Aryl Hydrocarbon Receptor (AHR). By purifying and cloning the AHR, Bradford’s lab not only became the central player in the understanding of how carcinogens act, but also contributed to the discovery that the AHR is a part of a large family of environmental sensor proteins, called PPARs, short for the founding members PPAR, AHR, and Sim.

Humans have 22 of these PAS proteins, most of which play important roles in our response to the environment. In general, these proteins that round the cell waiting for certain stimuli to occur, such as chemical exposure, changes in oxygen tension or changes in ambient light. When a person becomes exposed to any of a number of pollutants like dioxins, the AHR binds to its partner in the nucleus of a cell, when that cell can influence cancer response.

Bradford and his team study what happens when this receptor is activated and how this influences the carcinogenic reaction. “But more importantly, we want to know if what exists in the first place,” he says, “Why is there something in our bodies that allows harmful substances to affect us?”

How do the HPV vaccines work? To be fully vaccinated against HPV infection, patients need to complete three doses of the HPV vaccine: ideally over a six-month period. HPV vaccines offer the best protection for girls and boys who receive all three vaccine doses and have time to develop an immune response before becoming sexually active. Initiation of HPV vaccination is strongly recommended for girls and boys ages 11 - 12 years of age, but is also recommended for girls, ages 13 - 19 and for boys, ages 13 - 21 who have not yet been vaccinated.

The first HPV vaccine was approved for use in 2006 and for use in males in 2009. Since then, vaccine for boys, ages 13 - 21 who have not yet been vaccinated. The HPV vaccine is a great way to prevent a number of cancers, children need to be vaccinated before sexual activity and while the immune system is most responsive. As such, providers need to help parents recognize the importance of vaccinating their child by early puberty.

By increasing the use of the HPV vaccine as a cancer prevention vaccine, Wisconsin citizens lower their risk for some of the deadliest diseases of Wisconsin's children.

Amy Conlon, MPH, is the program director for the Wisconsin Comprehensive Cancer Control Program (WCCC). WCCC and its collaborators at the Wisconsin Cancer Council work to engage public, private and community partners to develop, implement and promote a statewide approach to reduce cancer rates in Wisconsin.

A HPV Vaccine Summit held on June 16, 2014 brought together advocates, health care providers and public health professionals from around the state to activate HPV vaccine champions across Wisconsin. Doctor recommendation is the strongest predictor of whether an adolescent gets the HPV vaccine. Doctors and other health care providers need to embrace every opportunity to vaccinate their patients. For many patients, it’s easier than ever to get the HPV vaccine. Because of the Affordable Care Act, most private health insurance plans will cover the HPV vaccine with no cost or deductible. In addition, the Vaccines for Children program provides vaccines for children 16 and younger who are under-insured, not insured, Medicaid eligible or American Indian/Alaska Native.

To provide the best protection against potential HPV-related cancers, children need to be vaccinated before sexual activity and while the immune system is most responsive. As such, providers need to help parents recognize the importance of vaccinating their child by early puberty.

Who is the AHR? The Aryl Hydrocarbon Receptor (AHR) is a receptor on the surface of cells. When this receptor is activated and how this influences carcinogenic reaction. “But more importantly, we want to know if what exists in the first place,” he says, “Why is there something in our bodies that allows harmful substances to affect us?”

While the answers to these questions are incomplete, recent studies from around the world suggest that AHR is really a part of an internal adaptive response that evolved to modulate the immune system. This recent discovery meant that the Bradford lab had to retool and become immunologists to understand AHR’s role in various diseases, or they could look for teammates. Choosing the latter, the Bradford lab has begun a meeting ground where colleagues from remarkably different backgrounds gather to develop a clearer picture of how humans respond to their chemical and physical environments, and how such adaptations influence human health.

“We are comprised of chemists, clinicians, epidemiologists, and molecular biologists – all making inroads together.”

“We could activate it only in the places where it prevents disease. Like the colon,” he says, “we could see how the mechanism to target agents to the places they will help.”

Other collaborators are approaching this complex question with broad scientific and clinical goals. Angela Wing, PhD, is studying how molecules bind to AHR in an attempt to design novel therapeutics, while Wei Xu, PhD, is researching how dioxins affect hormone production in the body. Epidemiologist Kristen Malacki, PhD, MPH and Javier Nieto, MD, MPH, PhD hopes to discover how these proteins mediate responses in human populations exposed to specific pollutants. Meanwhile, surgeon Josh Mandich, MD is examining the relationship between PAS proteins and organ transplant rejection.

It is a team with wide-ranging objectives, and one that is intimately involved with the problems patients face. While many people – chemists, clinicians, epidemiologists, and molecular biologists – all make inroads together, we are very different people. If the immune system is to remain healthy and be capable of detecting the growth of borderline resectable and locally advanced tumors, which are currently treated with chemotherapy, radiation therapy, and surgical therapy. The hope is that the immune system can be used to improve the ability of multimodality therapy to prolong overall survival for patients with this devastating cancer.