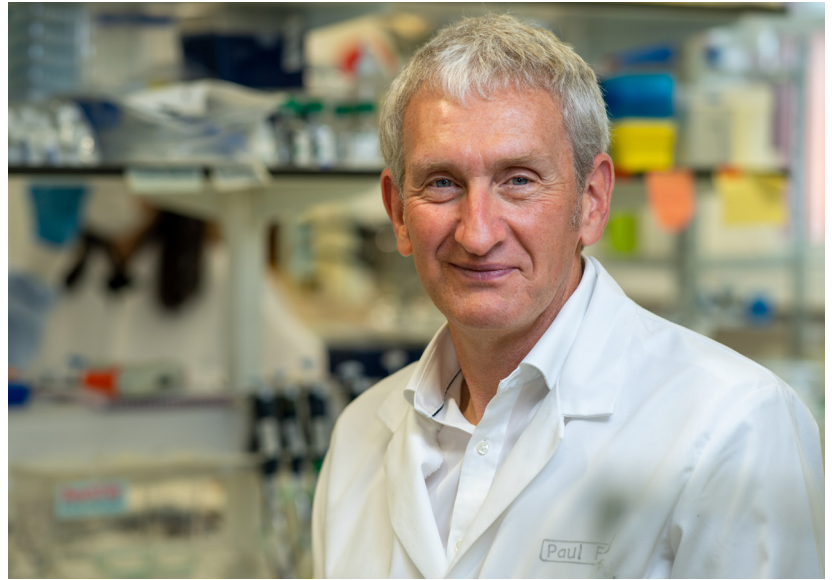


**PAUL FISH, PhD**

Professor and Head of Chemistry  
Alzheimer's Research UK UCL  
Drug Discovery Institute

*“An invaluable asset in working with our Harrington team is being able to have critical and supportive peer reviews as we develop this drug.”*



RE-ENFORCING A BARRIER TO

## PROTECT AGAINST ALZHEIMER'S

**FOCUS:** Restoration of healthy Wnt signaling to prevent and/or allay Alzheimer's disease.

With more than 50 million people worldwide living with Alzheimer's disease (AD), its tragic results are impacting countless lives. A therapy that halts or slows the progress of this disease is one of humankind's most significant unmet needs.

The blood-brain barrier (BBB) controls what nutrients get into the brain from blood (e.g. glucose that provides energy). With AD, the BBB no longer functions properly, and the brain receives insufficient glucose while allowing blood proteins to penetrate, causing inflammation. Preventing this loss of function could be a valuable therapeutic approach for AD.

“Wnt” are signaling proteins that are important in maintaining a healthy BBB, keeping nerve cells healthy, and promoting the clearance of toxic proteins like tau and amyloid.

Dr. Fish and his team have identified an enzyme at the BBB, called Notum, which prevents Wnt signaling by removing an essential palmitoleate group (fatty acid) from Wnt proteins. “We have found that Notum is increased in mouse models of AD and in post-mortem brain samples from AD patients,” Dr. Fish says.

“Thus, we hypothesize that inhibiting the increased Notum will help to restore Wnt signaling, the result being a healthy BBB in AD patients.”

Dr. Fish has indeed developed a potential drug that can inhibit Notum. He and his collaborators have reason to believe this drug may even have the potential for use in other conditions such as colorectal cancer. With insights from his Harrington Discovery Institute team, their drug is being rapidly progressed to testing in animal models of AD and safety studies to determine its suitability for treating AD patients.

### Harrington Discovery Institute

 University Hospitals | Cleveland, Ohio