Wylie Walker Vale Jr

(1941–2012)

Endocrinologist who deduced the molecular structure of stress hormones.

Wylie Vale and his colleagues answered a long-standing biological riddle: which substance controls the body's 'fight or flight' response? Vale's isolation of corticotropin-releasing factor (CRF) in 1981 and his exploration of the molecular basis of stress hormones opened the way to drugs for treating hypertension, heart disease, obesity, diabetes and depression.

With his passing at the age of 70, the worlds of physiology, neuroscience and peptide biology lost a charismatic leader. Vale effervesced with energy and curiosity, and loved big problems. He believed that life was neither fate nor serendipity, and viewed one's choice of friends, spouse, mentors and colleagues as the most important elements. Born and raised in Houston, Texas, Vale said that marrying his high-school sweetheart Betty was his first and best decision, and attending Houston's Rice University his next.

After his graduation in 1964, Vale pursued his PhD in physiology at Baylor University College of Medicine, also in Houston. His thesis work, completed in 1968, set him on a lifelong quest to dissect the neuroendocrine basis of physiology and behaviour. Vale's sense of adventure was piqued at Baylor by physiologist Roger Guillemin's new science of neuroendocrinology. In the late 1940s at the University of Montreal in Quebec, Canada, Guillemin had teamed up with Viennese physician Hans Selye, who proposed that stress was a specific biological phenomenon and had a neuroendocrine basis.

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In 1970, Vale and the Guillemin group moved to the Salk Institute in La Jolla, California. Around this time, with CRF proving too difficult to work on, they concentrated on characterizing other hormones. They reported the structure of the first hypothalamic peptide, thyrotropin-releasing hormone — comprising only three amino acids — highlighted in a landmark *Nature* paper in 1970. And in 1972 and 1973, the group described the factors controlling the release of follicle-stimulating hormone, luteinizing hormone and growth hormone — all key to human development. These results led to the 1977 Nobel Prize in Physiology or Medicine for Guillemin and Andrew Schally. Vale was in the audience at the Stockholm ceremony, and Guillemin said several times that he should have been on the stage with them.

Yet CRF, the pinnacle of hypothalamic theory, remained shrouded in mystery. The nature of CRF had been debated for decades, heightening its allure. Thought to be locked within the hypothalamus, it remained elusive because only tiny amounts could be extracted.

Vale was undeterred. In 1978, he announced to Guillemin in a handwritten letter that he would be leaving the lab and starting his own group to tackle CRF. He set up base camp in a single-storey wooden shack in the Salk Institute's car park. Armed with the latest high-performance liquid chromatography and gas-phase sequencing technologies, as well as thousands of sheep hypothalami, his team embarked on a game-changing expedition to isolate CRF and reveal its molecular structure.

When I arrived at the Salk Institute that year to study steroid and thyroid signalling mechanisms, I was attracted by luminaries such as Robert Holley, Francis Crick, Renato Dulbecco and Guillemin. But I soon found camaraderie in a motley crew of young scientists who met every Saturday morning for tennis and coffee — a tradition that lives on today. At that time, our group included Vale, virologist Inder Verma, and neurobiologists Jean Rivier and Stephen Heinemann, with the occasional guest appearance by tyrosine-kinase expert Tony Hunter. We became lifelong friends, collaborators and colluders, touring the world together in the frantic way that scientists do.

From the outset, it was clear that Vale was on a mission, betting his and his colleagues' careers on a risky gambit — one that in just three years yielded a picture of the crucial 41-amino-acid peptide and a view on to the vast landscape of the stress response it controls. Vale's 1981 breakthrough paper remains in the stratosphere of high-impact studies, and serves as a testimony to his vision and determination. Vale also parlayed his discoveries into two biotechnology companies, founding Neurocrine Biosciences in San Diego, California, and Acceleron Pharma in Cambridge, Massachusetts, to translate these findings into new drugs.

At 70 years old, Wylie was energetic and not ready to retire. He loved adventuring, hiking, slack-key guitar music and sharing a meal and an excellent bottle of wine with an irreverent group of co-conspirators while puzzling life's mysteries. After a lovely evening with friends at his home in Hana, Hawaii, he went to bed and never woke up. Wylie knew that no one was immune from life's slings and arrows, but he enjoyed great fortune and would not have begrudged even his own passing. ■

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