Revealing the Impact of Oxygen on Molecular Biology:
The Work of Howard Mason

The Oxidation of Catechol by Tyrosinase

Oxygen is one of the most abundant elements on Earth. It is also the element that unites the work of Howard Mason, a scientist most recognized for his characterization of oxidases in the 1950s. "He was really a great scientist, working very early on to try to understand how oxygen interacts with biological systems at the molecular level," says Judith Klinman at the University of California, Berkeley.

Mason’s most famous paper, “Mechanisms of Oxygen Metabolism,” was published in the journal *Science* in 1957. In it, Mason classified the different ways that enzymes can interact with oxygen during a reaction. The *Science* paper was preceded by “The Oxidation of Catechol by Tyrosinase,” published in the *Journal of Biological Chemistry* (JBC) in 1946. The JBC paper, which is being recognized as a Classic, provides an early glimpse into Mason’s life’s work on the ways oxygen can interact with substrates.

Working together at the National Institutes of Health’s Division of Industrial Hygiene, Mason and his co-author Charles Wright examined the oxidation of catechol for the production of the pigment molecule melanin. In a live cell, melanin’s precursor is made from the amino acid tyrosine through a series of steps in the presence of a copper-containing enzyme called tyrosinase. In laboratory experiments, however, melanin’s precursor can be made using catechol instead of tyrosine.

Previous studies had concluded that two atoms of oxygen were needed for catechol to be turned into the melanin precursor. However, by varying pH and concentrations of substrate and enzyme, Mason and Wright concluded in their JBC paper that three oxygen atoms were required. Through multiple oxidations, catechol transforms into a material that can polymerize into melanin.

Melanin fulfills various functions across many different organisms, such as helping to defend against infectious agents and preventing damage from ultraviolet light. Mason later worked out the pathway for melanin production in a series of three papers published in the JBC between 1947 and 1949. Because this pathway takes place *in vivo*, the starting material was tyrosine. The third paper contains a diagram, later dubbed the Raper-Mason scheme for melanogenesis, that illustrates the three steps of oxygen reduction necessary to obtain the melanin precursor. (Wright again was a co-author on this final paper.)

The pathway for melanogenesis is now known to be more complicated than the one that Mason presented in 1949. However, this work was an essential step toward understanding how melanin is formed. Before this body of work came out of Mason’s laboratory, molecular pathways had been determined genetically to find the enzymatic components.

With melanogenesis, Mason and colleagues showed that one enzyme catalyzed a reaction sequence, which in turn initiated a polymerization reaction that was partly enzymatic and
partly chemical. Dean Jones at Emory University, Mason’s former graduate student, describes
this work as “a synthesis of organic chemistry and enzymology, which was very special.”

After working out the pathway for melanin formation, Mason became interested in classi-
fying the different ways that oxygen can become reduced as biological substrates are oxidized. In his 1957 Science paper, Mason classified three types of enzymes: oxidases that transfer electrons to oxygen; mixed-function oxidases that incorporate one atom of atmospheric oxygen; and oxygenases that use two oxygen atoms. Today, mixed-function oxidases are commonly known as monooxygenases, and oxygenases are commonly referred to as dioxygenases.

Mason summarized the work that he contributed to in his curriculum vitae: “Small roots, giant tree: the discovery of heavy oxygen and its application to properties of oxidases and oxygenases have opened the respiratory phenomenon to a great variety and wealth of understanding and utility.”

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