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appear to be sensed by heme proteins, with subsequent transfer of electrons along a signal transduction pathway which may depend on reactive oxygen species. These heme-based sensors are generally two-domain proteins.

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During that time, his lab and Ratcliffe's lab independently found that the oxygen-sensing mechanism is present in all bodily tissues rather than only in the kidney, where EPO is produced. Kaelin and his lab

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then found that the protein VHL, named after the inherited syndrome von Hippel-Lindau's disease, was involved in controlling responses to hypoxia.

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