

GGC REPEAT EXPANSIONS AND THE DISCOVERY OF HIDDEN TOXIC PROTEINS

Trinucleotide repeat expansions are a well-established cause of over 60 genetic disorders, but their pathogenicity often remains a mystery when they occur in "non-coding" regions. While traditional models focus on RNA toxicity or loss of function, a new study published in *Nature Genetics* (1) reveals a surprising twist in the tale of Oculopharyngodistal Myopathy (OPDM) and Oculopharyngeal Myopathy with Leukoencephalopathy (OPML).

The researchers discovered that these GGC expansions are not actually in silent regions. Instead, they are embedded within previously unrecognized open reading frames. This means that sequences are translated into entirely new, toxic polyglycine-containing proteins. These new proteins aggregate into the p62-positive inclusions that are the hallmark of these diseases, directly causing muscle and neuronal degeneration.

1. <https://doi.org/10.1038/s41588-026-02507-z>