

## RNF216 gene

ring finger protein 216

### Normal Function

The *RNF216* gene provides instructions for making a protein that plays a role in the ubiquitin-proteasome system, which is the cell machinery that breaks down (degrades) unwanted proteins. Specifically, this protein functions as an E3 ubiquitin ligase. E3 ubiquitin ligases form part of a protein complex that tags damaged or excess proteins with molecules called ubiquitin. Ubiquitin serves as a signal to specialized cell structures known as proteasomes, which attach (bind) to the tagged proteins and degrade them.

The RNF216 protein tags proteins involved in an early immune response called inflammation to help control the response. RNF216 also regulates the amount of a protein in nerve cells (neurons) called Arc, which plays a role in a process called synaptic plasticity. Synaptic plasticity is the ability of the connections between neurons (synapses) to change and adapt over time in response to experience. This process is critical for learning and memory. It is likely that the RNF216 protein also regulates proteins involved in other body processes, although these proteins have not been identified.

### Health Conditions Related to Genetic Changes

#### Gordon Holmes syndrome

At least eight *RNF216* gene mutations have been found to cause Gordon Holmes syndrome, a rare condition characterized by reduced production of hormones that direct sexual development (hypogonadotropic hypogonadism) and difficulty coordinating movements (cerebellar ataxia). Many people with Gordon Holmes syndrome caused by *RNF216* gene mutations experience a decline in intellectual function (dementia). These mutations impair the ability of the RNF216 protein to tag unneeded proteins to be broken down. Impaired breakdown of Arc disrupts normal synaptic connections and plasticity, which likely contributes to dementia in people with Gordon Holmes syndrome. It is unclear how a lack of RNF216 protein function causes hypogonadotropic hypogonadism or cerebellar ataxia.

### Other Names for This Gene

- CAHH

- E3 ubiquitin-protein ligase RNF216 isoform a
- E3 ubiquitin-protein ligase RNF216 isoform b
- RING-type E3 ubiquitin transferase RNF216
- triad domain-containing protein 3
- TRIAD3
- U711
- UBCE7IP1
- ubiquitin-conjugating enzyme 7-interacting protein 1
- ZIN
- zinc finger protein inhibiting NF-kappa-B

## **Additional Information & Resources**

### Tests Listed in the Genetic Testing Registry

- Tests of RNF216 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=54476\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=54476[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28RNF216%5BTIAB%5D%29+OR+%28ring+finger+protein+216%5BTIAB%5D%29%29+OR+%28%28CAHH%5BTIAB%5D%29+OR+%28E3+ubiquitin-protein+ligase+RNF216+isoform+a%5BTIAB%5D%29+OR+%28E3+ubiquitin-protein+ligase+RNF216+isoform+b%5BTIAB%5D%29+OR+%28RING-type+E3+ubiquitin+transferase+RNF216%5BTIAB%5D%29+OR+%28TRIAD3%5BTIAB%5D%29+OR+%28ZIN%5BTIAB%5D%29+OR+%28triad+domain-containing+protein+3%5BTIAB%5D%29+OR+%28ubiquitin-conjugating+enzyme+7-interacting+protein+1%5BTIAB%5D%29+OR+%28zinc+finger+protein+inhibiting+NF-kappa-B%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D%29>)

### Catalog of Genes and Diseases from OMIM

- RING FINGER PROTEIN 216; RNF216 (<https://omim.org/entry/609948>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/54476>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=RNF216\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=RNF216[gene]))

## References

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## Genomic Location

The *RNF216* gene is found on chromosome 7 (<https://medlineplus.gov/genetics/chromosome/7/>).

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