| PublisherInfo | | |
|---|---|---|
| PublisherName | : | BioMed Central |
| PublisherLocation | : | London |
| PublisherImprintName | : | BioMed Central |

# Death domains, dysplasia and development

| ArticleInfo | | |
|---|---|---|
| ArticleID | : | 4282 |
| ArticleDOI | : | 10.1186/gb-spotlight-20011220-01 |
| ArticleCitationID | : | spotlight-20011220-01 |
| ArticleSequenceNumber | : | 353 |
| ArticleCategory | : | Research news |
| ArticleFirstPage | : | 1 |
| ArticleLastPage | : | 2 |
| ArticleHistory | : | RegistrationDate : 2001–12–20<br>OnlineDate : 2001–12–20 |
| ArticleCopyright | : | BioMed Central Ltd2001 |
| ArticleGrants | : | |
| ArticleContext | : | 130592211 |

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Edar is a member of the tumour-necrosis factor receptor (TNFR) family of signalling molecules that contains an intracellular death-domain. Mutation of the mammalian *downless* gene encoding Edar, or *Tabby* which encodes its ligand Eda, results in ectodermal dysplasia and defective morphogenesis. In the December 20/27 Nature, Headon *et al.* report characterization of the protein encoded by the mouse *crinkled* locus, a mutation in which results in hypohidrotic dysplasia identical to *Tabby* and *downless* mutants (*Nature* 2001, **414:**913-916). They performed positional cloning of the *crinkled* (*cr*) gene from *cr* x *Mus castaneous* backcrosses. Comparison of the syntenic regions of the mouse and human genomes led to the identification of a gene encoding a death-domain adaptor protein, named *EDARADD*. The human *EDARADD* gene is mutated in patients with autosomal hypohidrotic ectodermal dysplasia. The Edaradd protein interacts with the intracellular domain of Edar and resulted in activation of the signalling NFκB pathway. The *downless* and *crinkled* mutations abolish Edar-Edaradd interaction. This study defines a linear death-receptor pathway with a critical role in mammalian development.

# References

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2. *Nature*, [http://www.nature.com]