

URLs

DISEASE MODELS

Constructive connections

Diseases that occur in familial and sporadic forms present serious challenges to researchers, but lend themselves to the discovery of common biological pathways. This situation is exemplified by recent work on a fly model of Parkinson disease (PD), which has revealed a genetic link between the familial and sporadic forms of the disease.

The authors were drawn to a particular gene, *DJ1*, by its involvement in the familial form of PD, and went on to identify two close gene homologues in *Drosophila melanogaster* (*DJ1 α* and *DJ1 β*). Flies in which one or both of these genes were knocked out were viable and fertile; however, those that were exposed to toxins that influence sporadic PD — such as the herbicide paraquat and the insecticide rotenone — were strikingly more sensitive than normal animals. It's as though a lack of *DJ1* — in particular *DJ1 β* — renders organisms more susceptible to environmental toxins, leading ultimately to more rapid death, just as in sporadic PD in humans. *DJ1 β* also shifts to a more acidic form on exposure to these toxins; this isoform might therefore directly influence *DJ1* activity, setting up further research that could shed light into mechanisms of *DJ1* anti-oxidant function.

This work reinforces the usefulness of animal models for studying gene and environment interactions in human disease and proposes *DJ1* as an attractive drug target, given that the same pathway is probably

involved in both forms of PD. It also sets out goals for more research into this biological pathway — including resolving potential interactions between the two *DJ1* isoforms in protection from toxins, as described in an accompanying paper by Menzies and colleagues.

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References and links

ORIGINAL RESEARCH PAPER Meulener, M., Whitworth, A. J. & Armstrong-Gold, C. E. *et al.* *Drosophila* DJ-1 mutants are selectively sensitive to environmental toxins associated with Parkinson's disease. *Curr. Biol.* **15**, 1572–1577 (2005)

FURTHER READING Menzies, F. M. *et al.* Roles of *Drosophila* DJ-1 in survival of dopaminergic neurons and oxidative stress. *Curr. Biol.* **15**, 1578–1582 (2005)

