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The Structure of the Pro-domain of Mouse proNGF in Contact with the NGF Domain

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Nerve growth factor (NGF) is an important neurotrophic factor involved in the regulation of cell differentiation and survival of target neurons. Expressed as a proNGF precursor, NGF is matured by furin-mediated protease cleavage.

Increasing evidence suggests that NGF and proNGF have distinct functional roles. While the structure of mature NGF is available, little is known about that of the pro-domain because of its dynamical structural features.

We exploited an ad hoc hybrid strategy based on nuclear magnetic resonance and modeling validated by small-angle X-ray scattering to gain novel insights on the pro-domain, both in isolation and in the context of proNGF(1).

We show that the isolated pro-domain is intrinsically unstructured but forms transient intramolecular contacts with mature NGF and has per se the ability to induce growth cone collapse, indicating functional independence.

Our data represent an important step toward the structural and functional characterization of the properties of proNGF.

References

(1) R. Yan, H. Yalinca, F. Paoletti, F. Gobbo, L. Marchetti, A. Kuzmanic, D. Lamba, F.L. Gervasio, P.V. Konarev, A. Cattaneo, *A Structure*. **2019**, *27*, 78-89.

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