

Showcasing research from Professor Roland Sigel's laboratory, Department of Chemistry, University of Zurich, Switzerland.

Elucidating the solution structure of the monomolecular BCL2 RNA G-quadruplex: a new robust NMR assignment approach

G-quadruplexes (G4s) in 5'-untranslated regions of mRNA help regulate translation and are promising drug targets. Yet, their structural complexity and dynamic nature remain challenging to resolve. Here, we introduce a universally applicable NMR assignment strategy that exploits the architecture of G4 cores, using throughbond correlations to define G-tetrads. This enabled us to determine the solution structures of two mutants of the *BCL2* RNA G4, among the first natural monomolecular RNA G4s solved, revealing unexpectedly flexible sugar puckers and compact, well-defined cores, offering insights into RNA structure and guiding therapeutic development.

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