EDUCATION

B.S. (2004–2008)

Department of Materials Science, Faculty of Science, Kochi University

M.S (2008–2010)

Department of Chemistry, School of Science, Osaka University

Ph.D. (2010–2013)

Department of Chemistry, School of Science, Osaka University

RESEARCH AND PROFESIONAL EXPERIENCE

Posdoc (2013–2015)

Center for iPS Cell Research and Application, Kyoto University

Specially appointed assistant professor (2015–2018)

SANKEN (The Institute of Science and Industrial Research), Osaka University

Assistant professor (2018–Current)

SANKEN (The Institute of Science and Industrial Research), Osaka University

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Title:

A small molecule targeting UGGAA pentanucleotide repeat responsible for spinocerebellar ataxia type 31.

Abstract:

Spinocerebellar ataxia type 31 (SCA31) is an autosomal dominant spinocerebellar degenerative disorder caused by insertion of multiple pentanucleotide repeats containing d(TGGAA)$_n$, d(TAGAA)$_n$, d(TAAAA)$_n$ and a combination of two sequences d(TAAAATAGAA)$_n$ into the intron shared by genes of brain expressed associated with NEDD4-1 (*BEAN1*) and thymidine kinase 2. The inserted repeat sequence is transcribed into toxic r(UGGAA)$_n$, eventually resulting in RNA-mediated neurodegeneration through the formation of RNA foci accompanied with sequestration of RNA-binding proteins. In addition, either conventional translation or repeat-associated non-AUG (RAN) translation of r(UGGAA)$_n$ produces aggregates of pentapeptide (Trp-Asn-Gly-Met-Glu) repeat (PPR) proteins. The accumulation of RNA foci and PPR proteins has been observed in *Drosophila* models of SCA31 and the brain tissue of SCA31 patients. Recent studies showed that RNA-binding proteins such as TDP-43 and FUS directly bound to r(UGGAA)$_n$ and alleviated disease phenotype in *Drosophila* models of SCA31. These findings suggest that small molecules binding to r(UGGAA)$_n$ have potentials for reducing RNA toxicity. To this end, we explored a r(UGGAA)$_n$-binding small molecule from in-house chemical library. Here we report that a small molecule termed as naphthyridine carbamate dimer (NCD) binds to r(UGGAA)$_n$ and reduces RNA toxicity of SCA31 *in vivo*.