

Marike van Roon, PhD

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Nationality: Dutch

RESEARCH EXPERIENCE

2019-present	Medical Research Council Research Support Officer with Dr Nguyen
2017-2019	Medical Research Council Research Support Officer with Dr van Breugel
2013-2017	Medical Research Council Research Support Officer with Dr Lamers
2009-2013	Medical Research Council Career Development Fellowship (CDF).
2008-2009	Medical Research Council Research Associate
2007-2008	EMBO Long Term Fellowship (15% applicant success rate)
2005-2007	Marie Curie Intra-European Fellowship (11.6% applicant success rate)

- I contributed to obtaining the high resolution structure of human telomerase.
- I have worked in a team towards obtaining a high resolution structure of a human spliceosomal complex consisting of an RNA molecule and ten recombinant proteins.
- I solved the structures of 2 zinc-binding spliceosomal proteins by NMR and SF3b proteins Hsh49p in complex with part of Cus1p by X-ray crystallography.

1998-2004	PhD in Chemistry, Leiden University, the Netherlands (awarded 25-01-2005). Thesis title: <i>Schistosoma mansoni</i> : structural and biophysical aspects of Lewis X-antibody interactions (resulting in 8 publications).
1997	Summer research exchange program at Ithaca College, Ithaca NY, USA. Research topic: synthesis of fluoromethylfluorenes (resulting in 1 publication).
1996-1997	Ten months undergraduate research at Leiden University. Research topic: Synthesis of PNA and DNA analogues based on hydroxy-proline (resulting in 2 publications).

TECHNICAL SKILLS

Biochemistry	cloning, yeast and bacterial protein expression, insect cell and mammalian tissue culture, RNA in vitro transcription, protein purification using AKTA equipment and characterisation by standard methods, western blot.
Structural biology	automated liquid handling systems (mosquito, Caliper Sciclone i1000, Innovadyne screenmaker), high-throughput protein crystallisation, data collection (home and synchrotron sources), protein structure solution and analysis. NMR of oligosaccharides. EM grid making and screening.
Biophysical	SPR, DSF, CD, electrospray mass spectrometry, isothermal micro-calorimetry, fluorescence anisotropy.
Assay work	RNA splicing assay, RNA/DNA electromobility shift assay, ubiquitination assay, ELISA, DNA replication assays.
Organic chemistry	synthesis of complex oligosaccharides and peptide nucleic acid analogs.

SELECTED RNA RELATED PUBLICATIONS (for a full list see Appendix) AND POSTER PRESENTATIONS

- GE Ghanim, AJ Fountain, **AMM van Roon**, R Rangan, R Das, K Collins, THD Nguyen "Structure of human telomerase holoenzyme with bound telomeric DNA", **Nature**, 593 (7859), 449-453, 2021
- **AMM van Roon**, C Oubridge, E Obayashi, B Sposito, AJ Newman, B Séraphin, K Nagai "The crystal structure of U2 snRNP SF3b components: Hsh49p in complex with Cus1p binding domain". **RNA Journal**, 23, 968-81, 2017.
- **AMM van Roon**, YC Yang, D Mathieu, W Bermel, K Nagai, D Neuhaus "113Cd NMR experiments reveal an unusual metal cluster in the solution structure of the yeast splicing protein Bud31p". **Angewandte Chemie**, 54(16): 4861-4864, 2015.
- C Oubridge, Y Kondo, **AMM van Roon**, D Pomeranz Krummel, T Andreeva, K Nagai "Crystal structure of human U1 snRNP, a small nuclear ribonucleoprotein particle, reveals the mechanism of 5' splice site recognition" **Elife**. Jan 2;4. doi: 10.7554/eLife.04986, 2015.
- **AMM van Roon**, NM Loening, E Obayashi, JC Yang, AJ Newman, H Hernández, K Nagai and D Neuhaus "Solution structure of the U2 snRNP protein Rds3p reveals a knotted zinc-finger motif" **Proceedings of the National Academy of Sciences USA**, 105, 9621-9626, 2008

Research posters **RNA society meeting**, Berlin, Germany, 2008. Prize for best poster in the structural biology category.
Murnau conference, Murnau, Germany, 2010 The Modern RNA world,

EDUCATION

1993-1998 MSc Chemistry, Leiden University, Netherlands, Organic Chemistry
1987-1993 Melanchthon College, Rotterdam, the Netherlands. A-level equivalent: Chemistry, Physics, Mathematics, Biology, Dutch, English, French, Latin

APPENDIX Full list of publications

1. GE Ghanim, AJ Fountain, **AMM van Roon**, R Rangan, R Das, K Collins, THD Nguyen "Structure of human telomerase holoenzyme with bound telomeric DNA", **Nature**, 593 (7859), 449-453, 2021
2. S Baños-Mateos, **AMM van Roon**, UF Lang, SL Maslen, JM Skehel, MH Lamers "High-fidelity DNA replication in *Mycobacterium tuberculosis* relies on a trinuclear zinc center" **Nature Communications**, 8(1), 855, 2017
3. **AMM van Roon**, C Oubridge, E Obayashi, B Sposito, AJ Newman, B Séraphin, K Nagai "The crystal structure of U2 snRNP SF3b components: Hsh49p in complex with Cus1p binding domain". **RNA Journal**, 23, 968-81, 2017.
4. **AMM van Roon**, YC Yang, D Mathieu, W Bermel, K Nagai, D Neuhaus "113Cd NMR experiments reveal an unusual metal cluster in the solution structure of the yeast splicing protein Bud31p". **Angewandte Chemie**, 54(16), 4861-4864, 2015
5. C Oubridge, Y Kondo, **AMM van Roon**, D Pomeranz Krummel, T Andreeva, K Nagai "Crystal structure of human U1 snRNP, a small nuclear ribonucleoprotein particle, reveals the mechanism of 5' splice site recognition" **Elife**. Jan 2;4. doi: 10.7554/eLife.04986, 2015
6. DC de Geus, **AMM van Roon**, EA Thomassen, CH Hokke, AM Deelder, JP Abrahams "Characterization of a diagnostic Fab fragment binding trimeric Lewis X" **Proteins**, 76, 439-447, 2009
7. **AMM van Roon**, NM Loening, E Obayashi, JC Yang, AJ Newman, H Hernández, K Nagai and D Neuhaus "Solution structure of the U2 snRNP protein Rds3p reveals a knotted zinc-finger motif" **Proceedings of the National Academy of Sciences USA**, 105, 9621-9626, 2008
8. T. E. de Jongh, **AMM van Roon**, M. Prudêncio, M. Ubbink and G. W. Canters "Click-chemistry with an active site variant of azurin" **European Journal of Inorganic Chemistry**, 3861-3868, 2006
9. JAR Worrall, **AMM van Roon**, M Ubbink, GW Canters " The effect of replacing the axial methionine ligand with a lysine residue in cytochrome c-550 from *Paracoccus versutus* assessed by X-ray crystallography and unfolding" **FEBS Journal**, 272, 2441-2455, 2005
10. **AMM van Roon**, B Aguilera, F Cuenca, A van Remoortere, GA van der Marel, AM Deelder, HS Overkleeft, CH Hokke "Synthesis and antibody-binding studies of a series of parasite-specific fuco-oligosaccharides" **Bioorganic Medicinal Chemistry**, 13, 3553-3564, 2005.
11. **AMM van Roon**, KK Van de Vijver, W Jacobs, EA Van Marck, GJ van Dam, CH Hokke, AM Deelder "Discrimination between the anti-monomeric and the anti-multimeric Lewis X response in murine schistosomiasis" **Microbes and Infection**, 6: 1125-1132, 2004

12. **AMM van Roon**, HHJ Bink, JR Plaisier, CWA Pleij, JP Abrahams, NS Pannu "Crystal structure of an empty capsid of turnip yellow mosaic virus" **Journal of Molecular Biology**, 341: 1205-1214, 2004
13. **AMM van Roon**, NS Pannu, J.P.M. de Vrind, GA van der Marel, JH van Boom, CH Hokke, AM Deelder, JP Abrahams "Structure of an anti-Lewis X Fab fragment in complex with its Lewis X antigen." **Structure**, 12: 1227-1236, 2004.
14. A van Remoortere, HJ Vermeer, **AM van Roon**, JA Langermans, AW Thomas, RA Wilson, I van Die, DH van den Eijnden, K Agoston, J Kerekgyarto, JFG Vliegthart, JP Kamerling, GJ van Dam, CH Hokke, AM Deelder "Dominant antibody responses to Fuca1-3GalNAc and Fuca1-2Fuca1-3GlcNAc containing carbohydrate epitopes in *Pan troglodytes* vaccinated and infected with *Schistosoma mansoni*." **Experimental Parasitology**, 105: 219-225, 2003.
15. **AMM van Roon**, NS Pannu, CH Hokke, AM Deelder, JP Abrahams "Crystallization and preliminary X-ray analysis of an anti-LewisX Fab fragment with and without its LewisX antigen." **Acta Crystallographica Section D** 59 (7):1306-1309, 2003.
16. HF Koch , WC Pomerantz, EL Ruggles, M van Laren, **AM van Roon** "Comparing isotope effects and rates for the methanolic sodium methoxide reactions of 9-R-fluorene to those for p-CF₃C₆H₄CHClR (R = CH₂Cl, CH₂F and CF₃)." **Collection of Czechoslovak Chemical Communications** 67 (10): 1505-1516, 2002.
17. JC Verheijen, **AMM van Roon**, NJ Meeuwenoord, HR Stuivenberg, SF Bayly, L Chen, GA van der Marel, PF Torrence, JH van Boom "Incorporation of a 4-hydroxy-N-acetylprolinol nucleotide analogue improves the 3'-exonuclease stability of 2'-5'-oligoadenylate-antisense conjugates." **Bioorganic Medicinal Chemistry Letters** 10: 801-804, 2000.
18. JC Verheijen, **AMM van Roon**, AC van der Laan, GA van der Marel, JH van Boom "Synthesis of DNA-(3')-PNA chimeras with conformationally restricted linkers based on 4-hydroxyproline." **Nucleosides and Nucleotides** 18: 494-508, 1999.

I am a lab manager in the lab of Dr Kelly Nguyen at the MRC Laboratory of Molecular Biology (LMB) in Cambridge, UK. I joined Kelly when she moved to the LMB to establish her own lab in August 2019, so I was heavily involved in getting the lab up and running. The overall objective of the lab is to understand the molecular mechanisms of telomere maintenance and the roles of telomeres in human disease. We use a wide range of techniques in our studies from cryo-EM to obtain structural information to biochemical assays to study telomerase enzymatic activity and as quality control for our telomerase preps and *in vivo* studies in mammalian cells. Within a month I successfully ran the lab's first telomerase activity assay and maintained large scale mammalian tissue culture to obtain large amounts of human telomerase. After six months of starting the lab, the lockdown forced us to work from home, despite having to manage homeschooling of three young school-aged children as a single mum, I was able to help build the structure of the entire telomerase holoenzyme, including telomerase RNA, the telomerase reverse transcriptase (TERT) and the H/ACA RNP, into a high resolution cryo-EM map. In addition, we discovered histone H2A and H2B as novel telomerase components. To verify this finding, I performed immunoprecipitation assays with anti-histone H2A and H2B antibodies and found that we can pull-down telomerase activity with these antibodies. This work, which I co-first authored, has been published in Nature earlier this year.

I have always been fascinated by the structure and function of RNPs, so after my PhD I changed research direction and I applied for the prestigious Marie Curie and EMBO long term fellowships to study the structure and function of spliceosome in Kiyoshi Nagai's lab at the MRC LMB. I was granted both fellowships and moved to Cambridge to study the structure of yeast U2snRNP specific complexes SF3b and SF3b by protein crystallography. Unfortunately, the approach to reconstitute the entire complexes from recombinant proteins failed but I still solved and published the structures and performed biochemical assays with several spliceosomal proteins and I was awarded a prize for the best poster in the structural biology category of the RNA society meeting in Berlin, 2008. After my postdoc contract came to an end, I decided to try to get a permanent research position within the LMB to enable me to perform cutting edge scientific research whilst also having a good work/life balance to look after my three children. After working on DNA replication and the centrosome in Dr Lamers and Dr van Breugel's labs respectively I am very excited to be back in the RNA field in Kelly Nguyen's lab to study telomerase.