**Investigation of mutation types in Rett syndrome in Denmark**

**- Is long-time survival with *MECP2* mutations connected to type of mutation?**

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Objective: To investigate if long-time survival in individuals with Rett syndrome (RTT) and *MECP2* mutation is correlated to mutation types.

Methods: We looked at mutation types in patients known to the nation-wide Centre for Rett syndrome in Denmark and grouped them into patients<30 years, patients>30 years and deceased patients.

The mutations were categorized according to the study of Cuddapah et al.[1]. Here the authors concluded particular mutations p.Arg133Cys, p.Arg294X, p.Arg306Cys and 3' point mutations and truncations as being relatively mild mutations resulting in less RTT symptoms. The mutations p.Arg106Trp, Arg168X, p.Arg255X, Arg270X, splice site, deletions and insertions were categorized as giving severe RTT symptoms. Other mutations were the mutations categorized as giving a moderate phenotype or an unknown phenotype.

Results: The Danish RTT database included (July 2015) 98 alive and 18 deceased patients with *MECP2* mutations. Of 65 patients <30 years, 29% (19) had mild mutations, 40% (26) had severe mutations, and 31% (20) had other mutations. 33 patients >30 years, 52% (17) had mild mutations, 21% (7) had severe mutations, and 27% (9) other mutations. Amongst 18 deceased patients, 22% (4) had mild mutations, 44% (8) severe mutations, and 33% (6) other mutations.

Conclusion: Previous studies of *MECP2* mutations have shown that the type of mutation has some impact on disease severity. In this study we show that the type of mutation also has an impact on long-time survival and also a tendency to influence mortality.

[1] Cuddapah VA, Pillai RB, Shekar KV, Lane JB, Motil KJ, Skinner SA, Tarquinio DC, Glaze DG, McGwin G, Kaufmann WE, Percy AK, Neul JL, Olsen ML. Methyl-CpG-binding protein 2 (MECP2) mutation type is associated with disease severity in Rett syndrome. J Med Genet. 2014 Mar;51(3):152-8