Investigation of human TAAR1 (trace amine-associated receptor 1) brain expression

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TAAR1 (trace amine-associated receptor 1) is an emerging target in CNS diseases research, and data in genetic and non-genetic animal models are supportive to believe that TAAR1 agonists may play a role in psychiatric disorders. However, knowledge of human TAAR1 brain expression in the public domain is limited and analysis of the intronless TAAR1 is challenging. Here, we like to share and discuss results from a recent human TAAR1 expression study which was carried out using fresh frozen samples and formalin-fixed paraffin-embedded post mortem brain tissue from 5 donors (age at autopsy 61–69 years). Two brain areas, prefrontal cortex (PFC) and midbrain including ventral tegmental area/substantia nigra, were selected for next-generation sequencing (NGS), PCR, in situ hybridization and immunohistochemistry. All samples passed the quality control check and were suitable for analysis. No relevant TAAR1 signal was detected by NGS RNA-Seq and PCR analysis although the positive control using TARR1-overexpressing cells worked well. In situ hybridization (RNAcope technology) showed a low TAAR1 expression signal in the human pancreatic islets (positive control tissue) but no relevant TAAR1 expression in the brain areas selected. Immunohistochemistry staining with commercially available polyclonal TAAR1 antibodies resulted in specific staining in human TAAR1 overexpressing cells and in pancreatic islets but not in the human PFC and midbrain samples. In conclusion, we were unable to detect human TAAR1 brain expression in two brain areas, which is in contrast to our prediction and should encourage the discussion on human TAAR1 target engagement in CNS diseases.

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