mutation (40%) in the TCF4 gene located at 18q21.2 and encoding Transcription Factor 4. Variants in TCF4 usually occur de novo in children with severe phenotype, milder phenotypes inherited autosomal dominant We have examined 9 patients (4 boys and 5 girls) with Pitt-Hopkins aged 1 to 12 years.

Array-comparative genomic hybridization was performed in 5 children Target areas of the exome were investigated by massive parallel sequencing (NGS) in 4 cases. Validation of the identified variants was carried out by the Sanger method.

De novo microdeletions 1 revealed in 5 cases: arr 18q21.2q21.32 (51266708_56293087) ×1, arr 18q21.2 (52691678_52999165) ×1, arr 18q21.2q21.1 (50029734_61654329) ×1, arr 18q21.2q21.31 (51620900_54883094) ×1, arr18q21.2q21.31 (49493248_55403360) ×1. Detected deletions was from 307 Kb to 1162 Mb.

We identified 4 different mutations in the TCF4 gene in 4 patients with Pitt-Hopkins syndrome: c.961+2T>C, c.1452+1G>T, c.1634C>G, c.2033G>A.

Spectrum of mutations represented by splicing site mutations, nonsense and missense mutations.

All children had severe motor development delay and muscle hypotonia. Only one child was able to walk independently. All children had severe mental retardation. Expressive speech represented by vocalizations, individual words. Autistic and behavioral disorders were in 6 children. Severe episodes of hypertention followed by apnea observed in one child. Dysmorphic features included coarse face, protruding lower face, deep-set eyes, upsloping palpebral fissures, high, wide nose bridge, wide open mouth, cupid’s bow upper lip – thick, fleshy lips, cup-shaped ears. Three children diagnosed with myopia, scoliosis in one case. Brain MRI (in 4 children) show hypoplasia/dysplasia of the corpus callosum, atrophy/hypoplasia of the cerebellum, Dandy – Walker anomaly, hydrocephalus, small hippocampus size.

Conclusion Pitt-Hopkins syndrome is important for the differential diagnosis in children with severe mental retardation and behavioral disorders.

83 SCREENING FOR THE ACTIVITY OF HISTONE DEACETYLATION INHIBITORS IN THE GASTRULATING EMBRYO-DERIVED TERATOMA BIOLOGICAL SYSTEM

In our in vitro natural 3D biological system, rodent embryos explanted at the time of formation of the three germ-layers (gastrulation), develop a teratoma-like structure. We present the results of screening for the activity of Histone Deacetylase Inhibitors (HDIs) in this biological system.

9.5-days-old Fisher rat embryos-proper were cultivated for 14 days in Eagle’s MEM and 50% rat serum with 2mM or 1mM valproate or trichostatin A

(66 nM) at the air-liquid interface. Histone acetylation was assessed by western blotting and apoptosis and cell proliferation by immunohistochemistry and stereology. Spent media metabolomes were analyzed by IR-spectroscopy (FTIR).

Valproate and TSA both negatively influenced growth of explants and differentiation of the neural tissue. Valproate 2mM significantly increased histone acetylation and apoptosis in explants. In spent media metabolomes the amide I α-helices and the elevated ratio of A(CH3)/A(CH2, as biomarkers for histone acetylation, and a higher intensity of the 1625 cm⁻¹ vibrations of lipids at