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, arr 18q21.2q21.31 (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 hyperventilation followed by apnea observed in one child. Dysmorphic features included coarse face, protruding lower face, deep-set eyes, upslanting 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.

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RARE GENETIC SYNDROME PRESENTING AS COW MILK ALLERGY AND ECZEMA

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We describe here a case of an infant who applied initially for bronchiolitis and eczema and was afterwards diagnosed with 1q44 microdeletion syndrome.

The child was followed up in his early months of life for cow's milk allergy and related bronchiolitis and eczema. During the follow up persisting hypotonia and microcephaly began to be more evident. The face atypia was more prominent with frontal bossing, telecanthus, strabismus, small almond like eyes, flat nasal bridge. When the child got nearly 1 year old he came to the emergency department with a generalized febrile seizure, which afterwards followed with other febrile and nonfebrile seizures. In the mean time the child's general neuromotor development was very delayed with marked central hypotonia and low control of the head. In the laboratory investigations there was a persistent microcytic

anemia, despite oral iron replacement. The hemoglobin electrophoresis was normal. There was also noted slight hypothyroidism, which improved after a short time with hormone replacement therapy. The child underwent a cranial MRI which showed agenesis of corpus callosum. The infant was suspected of having a genetic syndrome and Molecular Karyotyping with Whole Genome Deletion/Duplication Analysis was performed. The result was consistent with a loss of 5,3 MB in the region 1q44 and a gain of 4,1 MB in the region 21p11.2q11.2.

Here, we present the first case of chromosome 1q44 deletion in Albania confirmed by microarray analysis. In literature, all reported patients showed growth and psychomotor retardation. In addition, many patients showed CNS anomalies, such as agenesis/thin corpus callosum or hydrocephalus, hypotonia, seizure, autonomic dysfunction, and feeding difficulties. In our case, brain MRI revealed partial agenesis of corpus callosum, delayed myelination, and seizures. We recommend orchypexy in order to prevent tumoral transformation of the testes.

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

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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 Deacetylation 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 absorption band for the parallel β -strand structure and CH₂ vibrations of lipids at