**0606**

**EXPRESSION SIGNATURE OF GENES ASSOCIATED WITH TELOMERE-TELOMERASE COMPLEX IN PATIENTS WITH MYELODYSPLASTIC SYNDROMES AND ACUTE LEUKEMIA: TEP1 GENE IS SURPRISINGLY UPREGULATED IN PROGRESSION OF MDS AND IN LEUKEMIC CELLS**

H. Zizkova,† S. Vcelikova,† J. Cermak,† J. Maaloufova,† R. Neuwirtova,‡ Z. Sieglova†

†Instit. of Hematology and Blood Transfusion, PRAGUE, Czech Republic; ‡First Medical Clinic Charles University, PRAGUE, Czech Republic

**Background.** Knowledge of dynamics of telomere-telomerase complex brings important sign into molecular background of leukemogenesis. Misbalance initiated by erosion of telomeres may affect also expression level of genes encoding in regulation of telomere length and telomerase activity. Thus, data on expression profiles of associated genes: hTERT encoding catalytic sub-unit of telomerase, the tankyrase (TNKS), TRF1 (Telomeric Repeat Binding Factor 1), POT1 (Protection Of Telomes 1), TEP1 encoding telomere associated protein, and myc may be valuable from the viewpoint of disease prognosis and monitoring of therapy effectiveness. **Aims.** To ascertain expression variations of genes involved in regulation of telomere-telomerase complex in patients with myelodysplastic syndromes (MDS), acute myelogenous leukemia (AML) from MDS, and primary untreated AML with the aim to evaluate their significance as prognostic factors of MDS evolution towards overt leukemia and markers of leukemic cells. **Methods.** The study was done on mononuclear bone marrow (BM) or peripheral blood (PB) samples from 42 patients with MDS, AML from MDS and untreated primary AML divided into subgroups according to the IPSS criteria. Mononuclear cells of 14 healthy BM or PB progenitor cells healthy donors served as normal controls. RNA was extracted using modified method of Chomczynski. Relative expressions of hTERT, TNKS, TRF1, POT1, TEP1, and myc RNA were assayed by real-time RTPCR with specific Taq-Man probes in RotorGene 3000A (Corbett Research) in comparison to expression of the housekeeping gene. Results. With the ratio more than 1.5 fold in comparison at healthy controls. Significance of molecular abnormalities responsible for AIP phenotype and the presence of clusters of mutations in particular geographic areas.

**0608**

**ASSOCIATION OF HUMAN PLATELET ALLOANTIGENS 1, HP2, HP3, HP4A, AND HP5 ALLELES AND GENOTYPES WITH SICKLE CELL ANEMIA**

W.Y. Almawi,† A.M. Al-Sabue,† N.A. Fawaz,‡ I.K. Al-Absi,† S.Saidi,§ N.Mahdi,§ K. Al-Ola†

†Arabian Gulf University, MANAMA, Bahrain; ‡King Faisal University, DAMMAM, Saudi Arabia; †University of Monastir, MONASTIR, Tunisia; §Salmaniya Medical Complex, MANAMA, Bahrain

**Background.** Insofar as sickle cell anemia (SCA) was described as a hemo-instable state where occultive vascular complications (OVC) and progression to stroke are frequently seen, polymorphisms of human platelet alloantigen (HPA) were reported as risk factors for several vascular abnormalities, including stroke. With the exception of a lone report documenting association of HPA-5b with SCA OVC, studies on potential association of HPA1 through HP5a with SCA are lacking. **Aims.** This study investigated the prevalence of HPA1, HPA2, HPA3, HPA4, and HPA5 alleles and genotypes among Bahraini SCA patients and control subjects. Linkage disequilibrium analysis will be used to investigate the disease association of the these polymorphisms. **Methods.** This was a case control study. Study subjects comprised 185 SCA patients (mean age 15.6±9.8) and 157 healthy controls (mean age 27.8±15.1); all were Bahraini nationals. Mutation analysis was assessed by PCR-SSP analysis. **Results.** Statistical analysis was performed on SPSS v. 13.0 statistics software, significance being set at p < 0.05. **Results.** The distribution of HPA2 (p=0.225) and HPA4 (p=0.075) genotypes were comparable between SCA patients and controls. In contrast, higher frequencies of HPA1 (p < 0.001), HPA5a (p=0.007) were found among controls, while HPA3b (p=0.034) and HPA5a (p < 0.001) alleles were more frequent in patients. Whereas HPA 3a/3a (p=0.036; RR=0.463) and HPA 5b/5b (p=0.001; RR = 1.082) were more prevalent among controls, HPA1b/1b (p<0.001; RR = 19.958), HPA 3b/3b (p=0.042; RR = 1.784), and HPA 5a/5b (p < 0.001; RR = 3.078) were significantly higher among SCA patients. **Summary/Conclusion.** Differential association of HPA phenotype with

---

**0607**

**TEN NOVEL MUTATIONS IN THE HMBS GENE RESPONSIBLE FOR ACUTE INTERMITTENT PORPHYRIA**

E. Di Pierro, V. Besana, V. Brancaleoni, S. Ausenda, D. Tavazzi, M.D. Cappellini

University of Milan-Policlinico Hospital, MILAN, Italy

**Background.** Acute intermittent porphyria (AIP) is an autosomal dominant disorder caused by a partial deficiency of hydroxymethylbilane synthase (HMBS), the third enzyme in the heme biosynthetic pathway. Clinical features of the disease are intermittent attacks of neurological dysfunction, including abdominal pain and neuropsychiatric symptoms. Diagnosis of AIP is often delayed, because it is more frequent in women than in men.**Aims.** To ascertain expression variations of genes involved in regulation of telomere-telomerase complex in patients with myelodysplastic syndromes complex in patients with myelodysplastic syndromes (MDS), acute myelogenous leukemia (AML) from MDS, and primary untreated AML divided into subgroups according to the IPSS criteria. Mononuclear cells of 14 healthy BM or PB progenitor cells healthy donors served as normal controls. RNA was extracted using modified method of Chomczynski. Relative expressions of hTERT, TNKS, TRF1, POT1, TEP1, and myc RNA were assayed by real-time RTPCR with specific Taq-Man probes in RotorGene 3000A (Corbett Research) in comparison to expression of the housekeeping gene. Results. With the ratio more than 1.5 fold in comparison at healthy controls. Significance of molecular abnormalities responsible for AIP phenotype and the presence of clusters of mutations in particular geographic areas.

**Results.** Notable increase of expression of hTERT, TEP1, and POT1 genes up-regulated already in early forms of MDS (p=0.0079) supports role of the POT1 gene as positive molecular regulator of telomerase. On the other hand, no relationships were found between POT1 expression and telomerase activity. Thus, data on expression profiles of associated genes: hTERT encoding catalytic sub-unit of telomerase, the tankyrase (TNKS), TRF1 (Telomeric Repeat Binding Factor 1), POT1 (Protection Of Telomes 1), TEP1 encoding telomere associated protein, and myc may be valuable from the viewpoint of disease prognosis and monitoring of therapy effectiveness. **Aims.** To ascertain expression variations of genes involved in regulation of telomere-telomerase complex in patients with myelodysplastic syndromes complex in patients with myelodysplastic syndromes (MDS), acute myelogenous leukemia (AML) from MDS, and primary untreated AML divided into subgroups according to the IPSS criteria. Mononuclear cells of 14 healthy BM or PB progenitor cells healthy donors served as normal controls. RNA was extracted using modified method of Chomczynski. Relative expressions of hTERT, TNKS, TRF1, POT1, TEP1, and myc RNA were assayed by real-time RTPCR with specific Taq-Man probes in RotorGene 3000A (Corbett Research) in comparison to expression of the housekeeping gene. Results. With the ratio more than 1.5 fold in comparison at healthy controls. Significance of molecular abnormalities responsible for AIP phenotype and the presence of clusters of mutations in particular geographic areas.

**Summary/Conclusion.** Differential association of HPA phenotype with

---

**TEN NOVEL MUTATIONS IN THE HMBS GENE RESPONSIBLE FOR ACUTE INTERMITTENT PORPHYRIA**

E. Di Pierro, V. Besana, V. Brancaleoni, S. Ausenda, D. Tavazzi, M.D. Cappellini

University of Milan-Policlinico Hospital, MILAN, Italy

**Background.** Acute intermittent porphyria (AIP) is an autosomal dominant disorder caused by a partial deficiency of hydroxymethylbilane synthase (HMBS), the third enzyme in the heme biosynthetic pathway. Clinical features of the disease are intermittent attacks of neurological dysfunction, including abdominal pain and neuropsychiatric symptoms. Diagnosis of AIP is often delayed, because it is more frequent in women than in men.**Aims.** To ascertain expression variations of genes involved in regulation of telomere-telomerase complex in patients with myelodysplastic syndromes complex in patients with myelodysplastic syndromes (MDS), acute myelogenous leukemia (AML) from MDS, and primary untreated AML divided into subgroups according to the IPSS criteria. Mononuclear cells of 14 healthy BM or PB progenitor cells healthy donors served as normal controls. RNA was extracted using modified method of Chomczynski. Relative expressions of hTERT, TNKS, TRF1, POT1, TEP1, and myc RNA were assayed by real-time RTPCR with specific Taq-Man probes in RotorGene 3000A (Corbett Research) in comparison to expression of the housekeeping gene. Results. With the ratio more than 1.5 fold in comparison at healthy controls. Significance of molecular abnormalities responsible for AIP phenotype and the presence of clusters of mutations in particular geographic areas.

**Results.** Notable increase of expression of hTERT, TEP1, and POT1 genes up-regulated already in early forms of MDS (p=0.0079) supports role of the POT1 gene as positive molecular regulator of telomerase. On the other hand, no relationships were found between POT1 expression and telomerase activity. Thus, data on expression profiles of associated genes: hTERT encoding catalytic sub-unit of telomerase, the tankyrase (TNKS), TRF1 (Telomeric Repeat Binding Factor 1), POT1 (Protection Of Telomes 1), TEP1 encoding telomere associated protein, and myc may be valuable from the viewpoint of disease prognosis and monitoring of therapy effectiveness.