EMBO 50 years
FEBS 50 1964–2014 ADVANCING MOLECULAR LIFE SCIENCES
SFBBM

the FEBS Journal

Volume 281 Supplement 1 September 2014 | ISSN 1742-464X www.febsjournal.org

FEBS EMBO

An anniversary conference

Paris 2014 hosted by SFBBM
30 August – 4 September

Abstracts

WILEY Blackwell

Local Organizing Committee

Chair : Frédéric Dardel

Executive coordinator : Xavier Coumoul

General Secretary : Alain Krol

Treasurers : Philippe Fossé, Maria Foka

FEBS/IUBMB liaison : Jacques H. Weil

Anniversary session : Guy Dirheimer

Bursaries : Laurence Drouard

Subsidies : Marylène Mougel

Abstracts : Christine Ebel

Communication : Marie Sissler

FEBS Young Scientists' Forum : Alice Verchère

Programme Committee

Susan M. Gasser, Basel (EMBO)

Angela Nieto, Alicante (EMBO)

Michael Reth, Freiburg (FEBS)

Eric Westhof, Strasbourg (SFBBM/FEBS)

and world-wide. PCa, compared to non-cancerous prostate tissue (NPT), contains various molecular alterations including aberrant expression of small non-coding RNAs. MicroRNAs (miRNAs) are 21–22 nt RNAs responsible for gene expression regulation and coordination of multiple physiological processes. In cancer, expression of various human miRNAs is markedly deregulated which causes subsequent changes in multiple cellular pathways and impacts disease outcome. The aim of this study was to identify differentially expressed miRNAs specific to PCa and suitable for early and non-invasive disease detection and prognosis.

Expression profile of 754 mature miRNAs was assessed using TaqMan Low Density Array (TLDA) cards A and B v3.0. Selected miRNAs were further analyzed with Custom Design TLDA cards to confirm the expression changes in an expanded set of samples. To evaluate miRNAs circulating in urine of PCa patients qPCR assays were applied.

In PCa tissues (N = 42), expression of 95 miRNAs significantly differed as compared to NPT samples (N = 12), 68 of them were up- and 27 downregulated. Comparison of miRNA profile in PCa cases with and without biochemical disease progression (BCR) revealed a marked upregulation of expression of 61 miRNAs. Based on the most significant differences between PCa and NPT and correlations with several clinicopathologic characteristics, 19 miRNAs were selected for further validation in the expanded set of samples. Significant upregulation of miR-19a, miR-21, miR-148a, and miR-375 was confirmed in PCa (N = 52) as compared to NPT (N = 12) samples, while expression of miR-340 was significantly increased in BCR-positive in comparison to BCR-negative cases. In further analysis, miR-19a and miR-21 were successfully quantified in urine collected from PCa (N = 137) and benign prostatic hyperplasia (BPH, N = 25) patients. Higher expression level of miR-19a was observed in PCa than in BPH, while in BCR-positive PCa cases both miR-19a and miR-21 were more abundant as compared to BCR-negative cases.

In conclusion, targeted inactivation of tumorigenic miRNAs might be considered as a novel treatment strategy for PCa. Non-invasive detection of selected miRNAs in urine might serve as a molecular tool for early identification of PCa.

Keywords: Prostate cancer, miRNA.

MON-034
Characterization of the cellular factors involved in microRNA destabilization by mouse cytomegalovirus

S. Cetin, G. Haas, M. Messmer, B. Chane-Woon-Ming, S. Pfeffer
Institut de Biologie Moléculaire et Cellulaire, Strasbourg, France

miRNA biogenesis and their functions have been extensively studied during the last decade, however less is known about the regulation of their stability. Nonetheless, an increasing number of examples illustrating the need to control mature miRNA stability (i.e. adaptation to biotic and abiotic stress) has emerged recently in the literature.

Our laboratory has previously discovered the destabilization of the cellular miR-27 upon mouse cytomegalovirus (MCMV) infection. A viral transcript (called m169), harbouring a functional miR-27 binding site, was found to be solely responsible of directing miR-27 for degradation [(1)]. High-resolution northern blot analyses and small RNA sequencing, demonstrated that the interaction between miR-27 and m169 induces the tailing and trimming of miR-27, a mechanism previously described in Drosophila and human cells [(2)].

While an extensive miRNA-target mRNA pairing seems to be a prerequisite to induce miRNA tailing and trimming, how this mechanism works or which factors are involved in this process is currently unknown. By using both MCMV infection and miR-27/m169 interaction as model systems, a biochemical approach based on the transfection of biotinylated-antisense oligonucleotides was used to induce the tailing-trimming of specific miRNAs and to pull down protein complexes for their analysis by mass spectrometry.

We identified novel factors that could be involved in the tailing-trimming of miRNAs, of which the roles of Terminal Uridylyl Transferase-1 (TUT1) and 3′-5′ exoribonuclease DIS3 like 2 (DIS3L2) proteins in the miRNA decay pathway will be discussed.

References

1. Marcinowski et al., PLoS Pathogene (2012).
2. Ameres et al., Science (2010).

Keywords: Degradation, microRNAs, Turnover.

MON-035
Clinical relevance of VKORC1 genotype and response to warfarin therapy

S. Karaca[1,2], M. Karaca[3], E. Cosgun[4], N. H. Aksoy[2], N. C. Bozkurt[5]
[1]Public Health and Genomics Research Center, GENAR Institute, Ankara, [2]School of Health Science, [3]Biology Department, Faculty of Science and Arts, Aksaray University, Aksaray, [4]Department of Biostatistics, Faculty of Medicine, Hacettepe University, [5]Department of Endocrinology and Metabolism, Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Turkey

Background: The management of warfarin therapy is challenging because it shows large inter and intra individual variability. The aim of current study was to characterize the effects of the *VKORC1* (−1639G>A) polymorphism and other personal characteristics on warfarin dose requirements in Turkish patients.

Methods: Unrelated 183 subjects with (n = 90 cases) and without (n = 93 controls) hemorrhagic complications during warfarin therapy were consecutively enrolled. MALDI-TOF based Sequenom MassARRAY platform was used for genotyping process. Multiple statistical analyses were performed to define the relation of VKORC1 variants with warfarin dose requirement, INR level, hemorrhage points, hemorrhage risk and severity, comorbidity and medications.

Results: The cases and controls did not have a significant difference in terms of VKORC1 (−1639 G>A) genotype distribution (p = 0.084). Frequencies were determined as 30.1%, 52,5% and 17.5% for AA, GA, GG genotype respectively. Allele distribution was 56.2% for (A) and 43.7% for (G) (HWE, p = 0.001) in the screened cohort. A multiple linear regression model revealed a strong relation between warfarin dose and age (p = 0.001), INR level (p = 0.001), hemorrhage risk (p = 0.02). The VKORC1 AA variant have significant association with higher INR (p = 0.01) and lower warfarin dose (mean dose was 3.37 ± 1.43 mg/day vs 5.75 ± 2.63 mg/day among cases) requirement (p = 0.001). The number of the cases with long term (>1 year) warfarin usage was higher, however, significant relation was not found between VKORC1 variants and treatment period.

Conclusions: VKORC1 −1639AA genotype is associated with lower warfarin dose and higher INR status and its frequency in the screened cohort was higher than it has already been reported for Turkish population. Determining the impact of genetic factors in a given population is important for research, development and implementation of personalized health care models which allows developing individualized pharmacological and medical follow-up advices and more targeted preventative healthcare strategies.

Keywords: drug metabolism, pharmacogenetics.