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Recent advances in the research and development for hereditary angioedema and evaluation of thromboembolic events following C1-inhibitor therapy

Hereditary angioedema (HAE) is a rare potentially life threatening disorder associated with a deficiency of functional C1-esterase inhibitor (C1-INH). HAE acute attacks are clinically manifested by swelling in the face, throat, abdomen and extremities and are more severe and frequent in female population than in men. Until recently, no HAE-targeted therapy was available in the United States. Since 2008, when the first plasma-derived C1-INH concentrate was approved by the US Food and Drug Administration (FDA), several HAE-specific therapies have been developed for the treatment of acute attacks and for prophylaxis. According to the available database and recent publications, C1-INH therapy in HAE patients is associated with a risk of thromboembolic events which is reflected in the prescribing information for C1-INH plasma products. Thrombosis also has been predominantly reported in women and appears to depend on hormonal status. These epidemiological suggestions prompted us to study mechanisms underlying the reports of thromboembolic events following C1-INH therapy. Our ongoing research project is supported by the FDA Office of Women's Health. This presentation will focus on current understanding of HAE mechanism(s), recent advances in the therapeutic development for HAE and our research efforts directed towards understanding key interactions between C1-INH and coagualtion systems, gender based diferences in C1-INH induced coagulation and the potential reasons for these diffences.

Recent Publications

1. Karnaukhova, E., Rutardottir, S., Rajabi, M., Wester Rosenlöf, L., Alayash, A.I., Åkerström, B. Characterization of heme binding to recombinant α1-microglobulin. Front. Physiol.5:465, 2014.
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3. Rutardottir, S., Karnaukhova, E., Nantasenamat, C., Songtawee, N., Prachayasittikul V., Rajabi, M., Rosenlöf, L.W., Alayash, A.I., Åkerström, B. Structural and biochemical characterization of two heme binding sites on α1-microglobulin using site directed mutagenesis and molecular simulation. Biochim. Biophys. Acta. 1864(1): 29-41, 2016.
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5. Hategan, A., Bianchet, M.A., Steiner, J., Karnaukhova, E., Masliah, E., Fields, A., Lee, M.H., Dickens, A.M., Haughey, N., Dimitriadis, E.K., Nath, A. HIV Tat protein and amyloid-β peptide form multifibrillar structures that cause neurotoxicity. Nat. Struct. Mol. Biol. 24(4):379-386, 2017.

Biography

Elena Karnaukhova is a Research Scientist in the Laboratory of Biochemistry and Vascular Biology, Center for Biologics Evaluation and Research, US Food and Drug Administration. She graduated with a PhD in Chemistry from Lomonosov Institute of Fine Chemical Technology (Moscow, Russia) where she subsequently became an Associate Professor. She was a Visiting Scientist at Leiden University (Holland), Medical University of Vienna (Austria) and CNRS (Orleans, France). In the US, she worked as a Senior Research Scientist at Columbia University (New York, NY) and Medical University of South Carolina (Charleston, SC). With her expertise in protein biochemistry and biophysical assessment, she serves as a reviewer for several scientific journals.

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