Резюмета на научните трудове след защита на дисертацията
на д-р Веселина Василева Узунова, дм

съгласно Приложение 8. 1.

(Минимални национални и допълнителни изисквания към научната и преподавателската дейност на кандидатите за придобиване на научна степен и за заемане на академичните длъжности "главен асистент", "доцент" и "професор" по научни области и/или професионални направления)

Публикациите и съответно резюметата са представени в хронологичен ред след защитата.

Публикация 1 (CV12):

A. Czogalla, E. P. Petrov, D. J. Kauert, V. V. Uzunova, Y. Zhang, R. Seidel and P. Schwille, Switchable domain partitioning and diffusion of DNA origami rods on membranes, Faraday Discuss. 161, 31 (2013)

Резюме:

Recently, DNA origami became a powerful tool for custom-shaped functional biomolecules. In this paper, we present the first approach towards assembling amphipathic three-dimensional DNA origami nanostructures and assessing their dynamics on the surface of freestanding phospholipid membranes. Our nanostructures were stiff DNA origami rods comprising six DNA helices. They were functionalized with hydrophobic cholesteryl-ethylene glycol anchors and fluorescently labeled at defined positions. Having these tools in hand, we could demonstrate not only the capability of the amphipathic nanorods to coat membranes of various phospholipid compositions, but also their switchable liquid-ordered/liquid-disordered partitioning on phase separated membranes. The observed translocation of our nanostructures between different domains was controlled by divalent ions. Moreover, selective fluorescent labeling enabled us to distinguish between the translational and rotational diffusion of our six helix bundles on the membranes by fluorescence correlation spectroscopy. The obtained data reveal how DNA origami can be employed as a valuable tool in membrane biophysics.

Публикация 2 (CV13):

W. Lin, F. V. Reddavide, V. V. Uzunova, F. N. Gür and Y. Zhang, Characterization of DNA-Conjugated Compounds Using a Regenerable Chip, Anal. Chem. 87, 848 (2015)

Резюме:

DNA-encoded chemical library (DECL) technology has emerged as a new avenue in the field of drug discovery. Combined with high-throughput sequencing, DECL selection experiments can provide not only many lead compounds but also insights into the structure−affinity relationship. However, the counts of individual DNA codes reflect, but cannot be used to precisely rank, the binding affinities of the corresponding compounds to protein targets. Herein, we describe a chip-based approach to realize an automated high-throughput assay for the

kinetic characterization of the interaction between DNA-conjugated small organic compounds and protein targets. Importantly, thismethod can be applied to both single-pharmacophore DECLs and self-assembled dual-pharmacophore DECLs.

Публикация 3 (CV14):

A. Czogalla, D. J. Kauert, H. G. Franquelim, V. V. Uzunova, Y. Zhang, R. Seidel, P. Schwille, Amphipathic DNA origami nanoparticles can scaffold and deform lipid membrane vesicles, Angew. Chem. Int. Edit. 54, 6501 (2015)

Резюме:

We report a synthetic biology-inspired approach for the engineering of amphipathic DNA origami structures as membrane-scaffolding tools. The structures have a flat membrane-binding interface decorated with cholesterol-derived anchors. Sticky oligonucleotide overhangs on their side facets enable lateral interactions leading to the formation of ordered arrays on the membrane. Such a tight and regular arrangement makes our DNA origami capable of deforming free-standing lipid membranes, mimicking the biological activity of coat forming proteins, for example, from the I-/F-BAR family.

Публикация 4 (CV16):

C. Lavilla, G. Yilmaz, V. Uzunova, R. Napier, C. R. Becer, A. Heise, Block-Sequence-Specific Glycopolypeptides with Selective Lectin Binding Properties, Biomacromolecules 18, 1928 (2017)

Резюме:

Glycopolypeptides with defined block sequences were prepared by sequential addition of two diff erent N-carboxyanhydrides (NCAs), followed by selective deprotection and functionalization of predefined positions within the polypeptide backbone. The sequential arrangement of the galactose units and the block-sequence length have been systematically varied. All the glycopolypeptides have been obtained with a similar overall composition and comparable molecular weights. Circular dichroism measurements revealed some dependence of the secondary structure on the primary composition of the glycopolypeptides at physiological pH. While statistical, diblock, and tetrablock glycopolypeptides adopted a random coil conformation, the octablock glycopolypeptide was mostly α-helical. The ability to selectively bind to lectins was investigated by turbidity measurements as well as surface plasmon resonance (SPR) studies. It was found that the extent of binding was dependent on the position of the galactose units and thus the primary glycopolypeptide structure. The octablock glycopolypeptide favored interaction with lectin RCA120 while the tetrablock glycopolypeptide demonstrated the strongest binding activity to Galectin-3. The results suggest that diff erent lectins are very sensitive to glyco coding and that precise control of carbohydrate units in synthetic polymeric glycopeptides will remain important.

Публикация 5 (CV17):

G. Yilmaz, V. Uzunova, M. Hartweg, V. Beyer, R. Napier and C. Remzi Becer, The effect of linker length on ConA and DC-SIGN binding of S-glucosyl functionalized poly(2-oxazoline)s, Polymer Chemistry 9, 611 (2018)

Резюме:

A new monomer, 2-[2-((2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylthio)propyl)]-2-oxazoline (Ac4Glc-S-Ox), was synthesized by direct addition of 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranose (Ac4Glc-SH) to 2-isopropenyl-2-oxazoline (iPOx) in the presence of solid butyl amine resin via a thiol–ene click reaction. The living cationic ring-opening polymerization was performed to prepare copolymers of Ac4Glc-S-Ox with 2-ethyl-2-oxazoline (EtOx). In order to systematically investigate the effect of the S-glucosyl substituent linked to the polymer backbone with different linkers on the cloud point and the binding ability, another series of glycopolymers was prepared by a post polymerization modification method. Copolymers of 2-decenyl-2-oxazoline and 2-butenyl-2-oxazoline with EtOx were first polymerized and then reacted with Ac4Glc-SH. The obtained glycopolymers exhibited lower critical solution temperature behavior that could be tuned easily by manipulating the alkyl linker length. Moreover, the binding results obtained using both turbidimetry and surface plasmon resonance techniques suggested that the relationship of the linker with the polymer backbone has a critical influence on glycopolymer–lectin binding behaviour.

Публикация 6 (CV18):

M. Riemer, V. Uzunova, N. Riemer, G. J. Clarkson, N. Pereira, R. Napier and M. Shipman, Phyllostictine A: total synthesis, structural verification and determination of substructure responsible for plant growth inhibition, Chem. Commun. 54, 7211 (2018)

Резюме:

The first total synthesis of phyllostictine A (PA) is reported, which confirms the structure of this fungal metabolite and its (6S,7R,8S)-stereochemistry. Both synthetic PA and an analogue containing the 5-methylene-1,5-dihydro-2H-pyrrol-2-one nucleus exhibit lM inhibitory activity in root growth assays against Arabidopsis thaliana, indicating that this heterocyclic subunit is key to the herbicidal activity of the natural product.

Публикация 7 (CV21):

V. V. Uzunova, A. Todev, J. Zarkos, D. Addai, J. Ananiev, P. Rashev, R. Alexandrova and A.Tolekova, Strengthening CoViD-19 therapy via combinations of RAS modulators, Med. Hypotheses 150, 110571 (2021)

Резюме:

Evidence has accumulated that the pathology of CoViD-19 is strongly related to the renin-angiotensin system (RAS). The blockage of the angiotensin converting enzyme 2 (ACE2) by the SARS-CoV-2 virus leads to downstream consequences such as increased vascular tone, extensive fibrosis and pronounced immune reactions. Different approaches to tackle the adverse viral effects by compensating the lost ACE2 function have been suggested. Here, we use an unequal-arm lever model to describe a simplified version of the biased regulation exercised by the angiotensin II and angiotensin-(1–7) hormones, which are the substrate and

the product of ACE2, respectively. We reason upon the lever dynamics and its disruptions caused by the virus, and propose that a combination of RAS modulators will most efficiently compensate the imbalance due to the excess of angiotensin II and the scarcity of angiotensin-(1–7). Specifically, we focus on the possible benefits of the simultaneous application of two agents, a MAS-receptor agonist and an angiotensin-II-type-2-receptor agonist. We conjecture that this combination has the potential to introduce a beneficial synergistic action that promotes anti-hypoxic, anti-fibrotic and anti-proliferative effects, thereby improving the clinical management of acute and chronic CoViD-19 pathologies.

Публикация 8 (CV23):

I. El Houari, P. Klíma, A. Baekelandt, P. Staswick, V. Uzunova, C. I. del Genio, W. Steenackers, P. Dobrev, R. Filepova, O. Novák, R. Napier, J. Petracšek, D. Inzé, W. Boerjan and B. Vanholme, Non-specific effects of the cinnamate-4-hydroxylase inhibitor piperonylic acid on auxin homeostasis, Plant J. 115, 470 (2023)

Резюме:

Chemical inhibitors are often implemented for the functional characterization of genes to overcome the limitations associated with genetic approaches. Although it is well established that the specificity of the compound is key to success of a pharmacological approach, off-target effects are often overlooked or simply neglected in a complex biological setting. Here we illustrate the cause and implications of such secondary effects by focusing on piperonylic acid (PA), an inhibitor of CINNAMATE-4-HYDROXYLASE (C4H) that is frequently used to investigate the involvement of lignin during plant growth and development. When supplied to plants, we found that PA is recognized as a substrate by GRETCHEN HAGEN 3.6 (GH3.6), an amido synthetase involved in the formation of the indole-3-acetic acid (IAA) conjugate IAA-Asp. By competing for the same enzyme, PA interferes with IAA conjugation, resulting in an increase in IAA concentrations in the plant. In line with the broad substrate specificity of the GH3 family of enzymes, treatment with PA increased not only IAA levels but also those of other GH3-conjugated phytohormones, namely jasmonic acid and salicylic acid. Finally, we found that interference with the endogenous function of GH3s potentially contributes to phenotypes previously observed upon PA treatment. We conclude that deregulation of phytohormone homeostasis by surrogate occupation of the conjugation machinery in the plant is likely a general phenomenon when using chemical inhibitors. Our results hereby provide a novel and important basis for future reference in studies using chemical inhibitors.