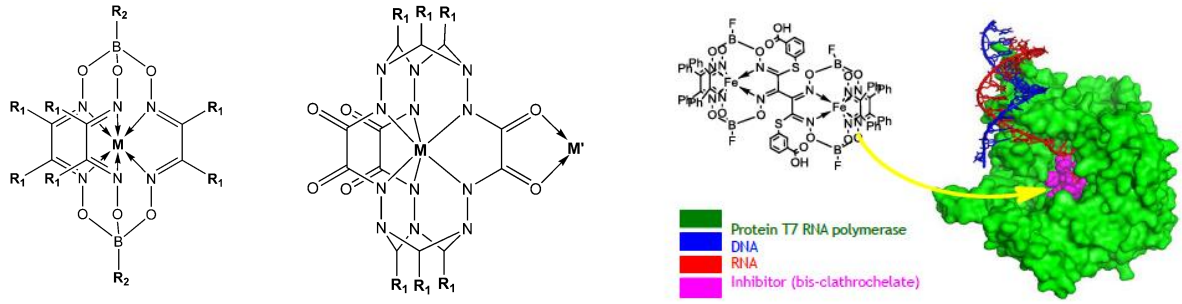
**International Research Staff Exchange Scheme (IRSES)**

# CAGEDRUGS: Design and elaboration of novel topological drugs based on cage compounds

**CAGEDRUGS** Project (2011-2015), supported by the Marie Curie IRSES Scheme of the 7th EU Framework Program (FP7-PEOPLE-2011-IRSES, grant 295160), brought together five research centres (*Faculty of Chemistry University of Wroclaw, UWR*, *Department of Chemistry Friedrich-Alexander-Universität Erlangen-Nürnberg, FAU, Department of Chemistry National Taras Shevchenko University, TSNUK, Nesmeyanov Institute of Organoelement Compounds Russian Academy of Sciences,INEOS RAS, and Vernadskii Institute of General and Inorganic Chemistry NAS of Ukraine, IGIC NASU)* devoted to the development of new nanomaterials for biomedical use based on macrobicyclic cage metal complexes (clathrochelates) [1, 2]. This joint exchange programme promoted and strengthened the complementarity of the participants and stimulated cross-fertilization, thus forming an excellent centre of synergy in research, innovation and technology in the area of functional nanomaterials. This network offered a complete training in the synthesis and characterization of new cage metal-containing materials for biomedical applications.

During the course of the project a series of new cltrhochelate compounds based on tris-dioximate (a) and tris-oxalodihydrazide (b) structures (Scheme 1) has been obtained. Their design, synthesis and physico-chemical characteristics, as well as biological activities were performed in five work packages (WP1: Design and template synthesis, WP2: Identification and structure studies, WP3: Spectral and physico-chemical characterisation, WP4: Reactivity and functionalisation, WP5: Biomedical applications of cage compounds).

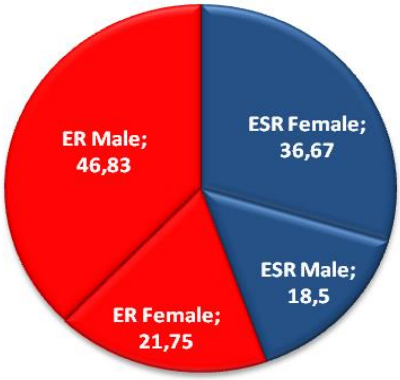



a b c

**Scheme 1**. Tris-dioximate (a) and tris-oxalodihydrazide (b) chathrochelates. Supramolecular binding of bis-clathrochelate Fe(II) as effective inhibitor of T7 RNA polymerase (IC50=500nM) to replicate fork by data of molecular docking (c).

The following main types of interactions between the macrobicyclic iron(II) complexes (clathrochelates) and biological systems were studied during this project: (1) their binding with globular proteins with formation of stable supramolecular assembles in which bulky three-dimensional clathrochelate molecules occupy hydrophobic cavity in the protein structures and additionally bind with them through multicentered interactions with polar functional groups. Binding to such transport proteins (albumins) plays an important role in the transport and detoxification of clathrochelates (their bioavailability); (2) inhibition of fibrillization by these three-dimentional macrobicyclic molecules; (3) "topological inhibition" of RNA and DNA transcriptions (Scheme 1c) by functionalized clathrochelates with suitable apical and ribbed substituents due to the formation of supramolecular assemblies of these clathrochelate inhibitors with macromolecular complexes “protein – matrix DNA – resulted RNA (DNA); (4) paramagnetic probes with record magnetic anisotropy. So, these cage complexes are promising for the search of potential antiviral and antitumor prodrugs, antifibrillogenic agents and paramagnetic probes for structural biology as well. Thus, macropolycyclic clathrochelate frameworks provide unique opportunities for the design of biologically active compounds, which are able to the transport in the living body due to specific protein-binding ability as well as to the formation of supramolecular assemblies with macromolecules and their complexes and to inhibition of various biological processes.

**Summary of CAGEDRUGS exchange**
(given in personmonths):




The joint research carried out in the frame of **CAGEDRUGS** Project was due to an efficient collaboration and mobility of researchers from five research teams, sharing their expertise, knowledge and best practice. The laboratory activities with learning by doing, planning of scientific activities, participation to scientific lectures/group discussions/workshops and networking activities were main elements of training of Early Stage Researchers (ESR) and transfer of knowledge among Experienced Researchers (ER) and ESR.
46 researchers (31 ESR and 15 ER) travelled between the five research centres in the frame of **CAGEDRUGS** Project spending in total 123.75 personmonths abroad on project activities. As international research driven network we were committed to increase gender representation among **CAGEDRUGS** researchers; among 46 scientists who took up secondments, 27 were females.

**CAGEDRUGS** Project visits, research, training and networking activity resulted in numerous new connections and contacts between the scholars from the different institutions. The individual participants got a unique opportunity to understand the whole chain from organic synthesis to biomedical studies applications. Knowledge transfer between EC/AC and TC teams has proven crucially important and has led to strengthening collaboration. In terms of benefits for ESR, it provided challenges for the scientific creativity of young researchers, especially important for further career perspectives.
The scientific data obtained has been reported in 21 scientific papers, numerous communications to the scientific society and several to the public (in the form of booklets, interviews, poster presentations at exhibitions, ect.). Among the target groups there were biochemists, medicinal chemists, molecular biologists, pharmaceutical industry. All the activities were summarized during the **CAGEDRUGS** Closing Workshop which took place in Wroclaw, Poland, 23-24 June 2015.


*CAGEDRUGS Closing Workshop, Wrocław, Poland, 23-24 June 2015.*

**Acknowledgements:** The **CAGEDRUGS** researchers would like to acknowledge the EU FP7 (2007-2013) for financial support (FP7-PEOPLE-2011-IRSES, grant 295160), and the staff of the participating institutions and REA for their assistance along the project.

References:
[1] http://cagedrugs.chem.uni.wroc.pl/
[2] Coordinator: Elzbieta Gumienna-Kontecka, D.Sc., Ph.D., Faculty of Chemistry, University of Wroclaw, e-mail: elzbieta.gumienna-kontecka@chem.uni.wroc.pl