Description for the General Public

Erythromycins and their derivatives (14-membered lactone macrolides) belong to the most effective and most successful antibacterial drugs used in medical therapy. Mechanism of their action is based on inhibiting of translation processes through their binding at ribosomes and steric blocking of ribosomal tunnel. At C(3) and C(5) erythromycin's ring and its derivatives there are: cladinose and desosamine, which are susceptible to hydrolysis process realize *via* bacteria (mechanism of resistance). The loss of these two parts (cladinose and desosamine) is reflected in destabilization of these macrolides' binding at ribosomes and results in decreased antibacterial activity. Within the project there are planned different modifications of erythromycin and clarithromycin with the use of highly economic cascade transformations, *click* chemistry reactions or metathesis in aim to attach different biomolecules for e.g. saccharides (and others) at C(3), C(5) and C(11) of 14-membered lactone ring *via* triazole or alkene's bridges, resistant to hydrolysis. Application of such chemical connections – triazole or unsaturated bridge (increase in lipophilicity) and attached saccharide (increase in water solubility) will give antibiotics with well-balanced physic-chemical parameters, what enable efficient transportation of the drug into the "target". Furthermore, increasing in bulkiness arms at C(3), C(5) and C(11) at 14-membered lactone rings may be reflected for better stabilization of the synthesized antibiotics at the binding site *via*, unavailable up to now, interactions with nucleotide base pair region 2504-2507 (desosamine is to short substituent) or *via* filling the gap between L4, L22 i L37E subunits at ribosomes, similarly as for extremely active antibiotics of telthromycin group. Chemical transformations planned within the project will expand the basic knowledge about chemistry of 14-membered macrolide antibiotics and could gave promising efficient alternatives antibacterial agents to currently-used erythromycins and their derivatives in therapy against bacterial infections.

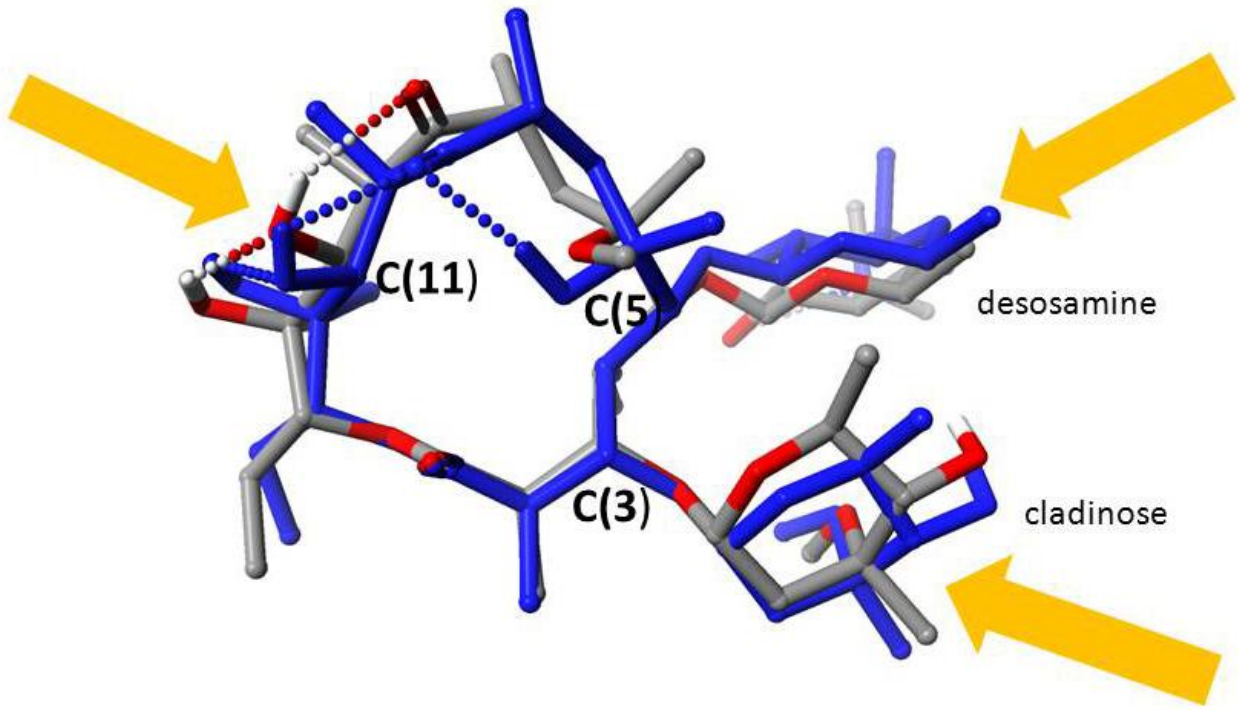

Fig. 1 Superimposed structures of 14-membered lactone macrolides: erythromycin (blue) and clarithromycin (grey), and considered sites of modifications (incorporation of resistant to hydrolysis arms).