LIFE SCIENCES

Production and research of recombinant viral and human proteins in yeast

Vilnius University

Keywords: *recombinant proteins, diagnostics, ELISA, nucleocapsid protein, virus-like particles, S. cerevisiae*

Research group activities

The activities of the research group addresses studies related to efficient production of recombinant viral and human proteins in yeast cells by improvement of expression systems and yeast genetic background. Despite that yeast Saccharomyces cerevisiae frequently serves as a reasonable host for heterologous protein expression, in many instances, it is far from optimal. Our aim is to understand and balance processes in yeast trigged by synthesis of recombinant proteins, such as unfolded protein response, identify factors necessary for efficient recombinant protein expression by overexpression or deletion of target genes. In an attempt to elucidate the requirement of factors for the biosynthesis of recombinant viral and human proteins we use proteomics, yeast mutant and gene collection studies, substitution of some yeast chaperones by human homologues. The group is also interested in search and characterization of new polyomaviruses, studies of virus-like particles (VLPs) formation, recombinant human chaperones, and protein engineering based on construction of chimeric VLPs harboring foreign epitopes. We employ hamster polyomavirus VLPs as carriers for short and non-immunogenic protein sequences with are presented on VP1 VLPs to increase their immunogenicity. For presentation of large and complex protein molecules (as single chain antibody molecules) we use VP1/VP2 VLPs.

We have a wide network of international collaboration and long-lasting experience in conducting collaborative projects with industrial partners.

Proposal

We offer our expertise in production and characterization of recombinant viral (polyomavirus, papillomavirus, paramyxovirus) and human proteins (calreticulin, BiP) in yeast, generation of chimeric virus like particles harboring foreign epitopes, studies on the design of different expression systems in yeast or construction of yeast strains.

We are interested in new joint projects and collaboration with industrial and academic partners.

Meet our team

Head: Prof. Dr. **Alma Gedvilaite**

Team members: senior scientist Dr. Rimantas Slibinskas

Scientists: Dr. Evaldas Ciplys, Dr. Danguolė Žiogienė

Technician: Monika Valavičiūtė

PhD students: Milda Norkienė, Edita Bakūnaitė, Rūta Zinkevičiūtė, Neringa Macijauskaitė, Eimantas Žitkus.

Research outcomes

- Large collection of more than 40 different virus like particles (VLPs) derived from various polyomavirus (all 13 human polyomavirus, rodents, avian and other host polyomavirus) VP1 proteins and papillomavirus L1 proteins (HPV16, 18, 31, 33), nucleocapsid proteins of different paramyxoviruses (mumps, measles and others), porcine circovirus type 2 capsid proteins (see selected publications 1, 2, 3).
- Yeast expression systems for construction and production of hamster polyomavirus VP1 and VP1/VP2 VLPs as carriers harboring non immunogenic peptides or complex molecules of interest (see patent and selected publication 4).
- Yeast produced and secreted human proteins calreticulin and BiP (see selected publication 5).
- Genetic engineered yeast strain collection for recombinant protein production.
- Participation in EU-funded Framework 6 projects, coordination and participation in research projects supported by European Social Fund the Lithuanian Science Council.
- Collaborative projects and contracts with biotech companies Thermo Fisher Scientific Baltic, Abcam Ltd (UK), and others.
- Long lasting collaboration with researchers from Friedrich-Loeffler-Institute (Germany), Health Protection Agency (UK).
- Over 50 publications in peer-reviewed journals

Patent and most important publications:

- **Žvirblienė A., Gedvilaitė A., Ulrich, R., Sasnauskas.** Process for the production of monoclonal antibodies using chimeric VLPs. US Patent No.:US7,919,314 B2. Apr. 5, 2011.
- **Norkienė M, Stonytė J, Žiogienė D, Mažeikė E, Sasnauskas K, Gedvilaitė A.** Production of recombinant VP1-derived virus-like particles from novel human polyomaviruses in yeast. BMC Biotechnology. 2015, 15:68. DOI: 10.1186/s12896-015-0187-z
- **Nainys J, Lasickienė R, Petraitytė-Burneikienė R, Dabrisius J, Lelesius R, Sereika V, Žvirblienė A, Sasnauskas K, Gedvilaitė A.** Generation in yeast of recombinant virus-like particles of porcine circovirus type 2 capsid protein and their use for a serologic assay and development of monoclonal antibodies. BMC Biotechnology 2014 14:100. doi:10.1186/s12896-014-0100-1 847
- **Slibinskas R., Samuel D., Gedvilaitė A., Staniulis J, and Sasnauskas K.** Synthesis of the measles virus nucleoprotein in yeast Pichia pastoris and Saccharomyces cerevisiae. J Biotechnol. 2004 v. 107, n.2, p. 115-124.
- **Plečkaitytė M, Žvirblienė A, Šėžaitė I, Gedvilaitė A.** Production in yeast of pseudotype virus-like particles harboring functionally active antibody fragments neutralizing the cytolytic activity of vaginolysin. Microb Cell Fact. 2011. 10:109. doi: 10.1186/1475-2859-10-109
- **Čiplys E, Žitkus E, Gold LI, Daubriac J, Pavlides SC, Højrup P, Houen G, Wang WA, Michalak M, Slibinskas R.** High-level secretion of native recombinant human calreticulin in yeast. Microb Cell Fact. 2015;14:165. doi: 10.1186/s12934-015-0356-8.

Resources

The facilities are well equipped for microbiology, genetic engineering, and molecular biology work and protein purification. The special equipment includes: transmission electron microscope Morgagni 268 (FEI Inc.), ultracentrifuges (Beckman), equipment for nanoparticle tracking analysis NanoSight LM10-HS(NanoSight) and high resolution 2D electrophoresis.

Contacts

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