NORUSCASA seminars:
"Functional Metagenomics for discovery of bioactive compounds"

Date and time: February, 2022; 17:00-18:30 am CET
Venue: Teams; Click here to join the meeting

In the frame of Research Council of Norway project NORUSCASA (previously connected to DLN through the INBioiPharm project), SINTEF and NTNU cordially invite interested students and researchers to the third seminar occasion in the NORUSCASA seminar series.

We are looking forward to welcoming you to 2 exciting lectures and vivid discussions!

17:00h CET - Dr David Mead, Varigen Biosciences, USA:

New Tools For Targeted Cloning And Over Expression Of Biosynthetic Gene Clusters

105 biosynthetic gene clusters (BGCs) ranging 12 to 130 kb from 95 diverse bacterial and fungal strains were successfully captured and cloned using CRISPR-Cas9 to precisely excise the pathway of interest. To improve the success of heterologous expression, we developed a new *Streptomyces* and *Bacillus* BGC expression vector (pDualP) which uniquely includes two inducible promoter elements, one flanking each side of the cloning site. As a proof of concept, we cloned the ACT and RED BGCs from *S. coelicolor* in both orientations of the pDualP vector, integrated them into *S. lividans* ΔredΔact, and observed inducible production of the blue ACT cluster product and the red RED cluster product but not from the native promoters. Second, we observed a substantial enhancement of the antimicrobial activity of heterologously-expressed, soil-derived metagenomic BGCs through induction with pDualP. Expression cloning of nystatin, vancomycin, and several other metabolites was successful. We also de-orphaned the stravidin BGC from *Streptomyces* sp. NRRL S-98 using the same approach and showed heterologous bioactivity of the bacillusin A metabolite against MS+RA. These results indicate that virtually any sequenced BGC can be cloned intact from complex genomes, and that direct cloning to a dual-inducible expression vector can greatly accelerate downstream small molecule characterization.

17:40h CET – Dr Lonnie van Zyl, University of Western Cape, South Africa:

Natural product discovery at IMBM: Metagenomics and more

We describe the efforts at IMBM to identify and characterize individual genes or pathways responsible for producing metabolites that could have clinical or industrial use, either through metagenomic techniques or traditional culturing and cloning approaches. Examples to be discussed include the isolation of an ornithine lipid synthase for production of ornithine lipid and lyso-ornithine lipid as well as the cloning and expression of two novel putative lipopeptide encoding pathways in *E. coli.*