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PedA-1, since their specific receptor Man-PTS is not present on its inner membrane. In addition, an *sdaC* mutant *E. coli* strain was employed as a receptor-free host for MccV, as it does not express SdaC, the specific membrane receptor for this microcin. If the fusion EtpM-bacteriocin kills the expressing host cell, it would mean that the specific receptor could be dispensable for the final step of membrane disruption. As these constructs exert a lethal effect when they are expressed, they are called "suicide probes". This hybrid proteins EtpM-Bacteriocins were heterologeously expressed in *E. coli* and *E. coli* ΔsdaC respectively, and the results suggest that, indeed, the specific receptor would act simply as docking molecule and it would not participate in pore formation mechanisms. The effect of these suicide probes in some membrane properties is also analyzed.

Keywords: bacteriocin, mechanism, receptor, microcin, antibiotic

(1844) **DISSECTION OF VIRULENCE-ASSOCIATED TRANSCRIPTIONAL NETWORKS IN *Brucella*: SEEKING FOR NEW REGULATORY PROTEINS THROUGH BIOINFORMATIC, BIOCHEMICAL AND MOLECULAR APPROACHES**

Gabriela Sycz, Rocío Tau, Hernán Bonomi, Angeles Zorreguieta, Rodrigo Sieira
Fundación Instituto Leloir.

In facultative intracellular bacteria of the genus *Brucella*, significant progress has been made in identifying virulence factors. However, the genetic program orchestrating the *Brucella* intracellular adaptation process is still poorly understood. In this regard, our group recently identified the regulon of VjbR, a transcription factor known to play a major role in the pathogenesis of *Brucella*. Our ChIP-seq and RNA-seq analyses showed that VjbR controls bacterial functions relevant for survival during the initial stages of the intracellular infection, and revealed that VjbR indeed acts as a global regulator exhibiting a large amount of binding sites across the *Brucella* genome. However, further analysis of our data indicated that the VjbR transcriptional network is highly complex. For instance, we found that VjbR failed to bind to many genomic positions containing conserved VjbR-binding motifs, which suggested the possible existence of competitors that prevent binding of VjbR to specific promoters under the assayed conditions. To explore this possibility, we developed a bioinformatic method that allowed us to identify conserved sequences adjacent to VjbR-binding motifs that failed to bind VjbR *in vivo*, which could act as binding sites for competitor transcription factors. EMSA analysis of one of such specific promoters showed that in the absence of competitors, VjbR alone was able to interact *in vitro* with its target DNA sequence. Moreover, in *Brucella* crude extracts we detected two proteins able to bind to the analyzed promoter. Using biochemical and molecular methods we isolated one of these proteins, wich was identified as a transcription factor known to coactivate expression in other direct targets of VjbR. Determination of the second DNA-binding protein, however, will requiere further work. In summary, here we present a pipeline suitable to identify possible competitor and/or coactivator transcription factors in complex transcriptional regulatory networks.

Keywords: transcriptional regulation, functional genomics, LuxR, bacterial pathogen

(849) **CHARACTERIZATION OF SECONDARY METABOLITE BIOSYNTHESIS PATHWAYS IN *S. EUROCIDICUS*.**

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Streptomyces eurocidicus produces at least three secondary metabolites, azomycin, eurocidin and tertiomycin, which its biosynthesis pathways are unknown. Azomycin is a broad-spectrum antibiotic belonging to the group of nitroheterocyclic compounds. Eurocidin is a pentaene macrolide with antifungal activity. And Tertiomycin is an antibacterial compound from the spiramycin family with activity against Gram-positive bacteria, but the structure is still unknown. With the aim of study the biosynthetic pathwayof these metabolites, we have first validated the production of each of the using *S. eurocidicus* NRRL B-1676 strain. In liquid media culture it was found that eurocidin is produced in the exponential phase while both azomycin and tertiomycin are produced in the stationary phase of growth. Surprisingly, it was found that *S. eurocidicus* has a compound, presumably eurocidin, with a strong fluorescence that stains colonies on solid and liquid media. The identity of each compound was determined by TLC observed by UV at 254/302 nm and by p-anisaldehyde staining, or by high resolution LC-MS. In turn, the activities of each spot observed were determined by inhibition against *Bacillus subtilis* or *Saccharomyces cerevisiae*. Then, we have sequenced the *S. eurocidicus* NRRL B-1676 genome by 100bp paired-end reads using Ilumina technology. Analysis of the genome sequence allowed identifying putative gene cluster for each metabolite using bioinformatic tools. To validate these gene clusters we are constructing knock-out strains by homologous recombination or by UV mutagenesis. Thus, mutant strains for eurocidin gene cluster were obtained and it was found that they lost antifungal activity and are not fluorescent. New mutant strains for the other pathways are being constructed.

Keywords: Streptomyces, Azomycin, Eurocidin, Tertiomycin, Pathways.

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(554) **A FUNCTIONAL CHARACTERIZATION OF AMP-ACTIVATED PROTEIN KINASE IN *Trypanosoma cruzi***

Tamara Sternlieb, Patricio Dino Genta, Alejandra Cecilia Schoijet, Nadia Maricel Barrera, Milena Massimino Stepñicka, Guillermo Daniel Alonso
INGEBI - CONICET - UBA

The AMP-activated protein kinase (AMPK) is a heterotrimeric enzyme involved in maintaining energy homeostasis in response to different stresses in many organisms. Sequence and structure of its subunits may change between organisms, but they maintain the same function. The α subunit contains a N-terminal kinase catalytic domain, the β subunit acts as a scaffold and intervenes in the localization of the complex and the γ subunits binds AMP. During the transition from the mammal host to the insect vector, *Trypanosoma cruzi* suffers nutritional stress from the absence of glucose in the insect's midgut. The ability to respond to this stress, allows the parasite to differentiate and survive. Recently, it was shown that *Trypanosoma brucei* AMPK is involved in surface protein expression changes in response to nutritional stress and differentiation.

We identified four candidate genes for the AMPK subunits of *T. cruzi* (α1, α2, β and γ). Each of these subunits was capable of reverting the 'glucose dependent' phenotype of *S. cerevisiae* conditional mutants alternatively lacking one subunit of the AMPK ortholog SNF1. Also, we overexpressed the α1, β and γ subunits with a hemagglutinin (HA) Tag in CL Brener epimastigotes and evaluated their localization and possible post-translational modifications. Western blots using anti-PhosphoAMPK antibody showed specific stripes corresponding to the expected MW of the alpha subunits. These stripes are reduced in intensity or completely deleted with Lambda phosphatase treatment. Also, epimastigotes treated with an AMPK specific activator show a shift in the intensity pattern of the stripes. Thus, the phosphorylation pattern of the α subunits can be modified *in vivo*. RT-PCR assays also revealed the endogenous α2 mRNA, but not the α1 mRNA in epimastigotes. Our results show, for the first time, the presence of an AMPK ortholog in *Trypanosoma cruzi*. In the future, we aim to discover its role in the life cycle and stress responses of this parasite.

Keywords: AMPK, stress response, AMP, signaling, transduction pathway

(608) **IN VIVO EVALUATION OF THE BIOLOGICAL FUNCTION OF AN AMP-ACTIVATED PROTEIN KINASE ALPHA SUBUNIT IN *TRYPANOSOMA CRUZI***

Patricio Dino Genta, Tamara Sternlieb, Nadia Maricel Barrera, Milena Massimino Stepñicka, Guillermo Daniel Alonso, Alejandra Cecilia Schoijet