AMYLOID-LIKE β-AGGREGATES AS FORCE-SENSITIVE SWITCHES IN FUNGAL BIOFILMS AND INFECTIONS

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Summary: Cellular aggregation is an essential step in the formation of biofilms, which promote fungal survival and persistence in hosts. In many of the known yeast cell adhesion proteins, there are amino acid sequences predicted to form amyloid-like β-aggregates. These sequences mediate amyloid formation in vitro. In vivo, these sequences mediate a phase transition from a disordered state to a partially ordered state to create patches of adhesins on the cell surface. These β-aggregated protein patches are called adhesin nanodomains, and their presence greatly increases and strengthens cell-cell interactions in fungal cell aggregation. Nanodomain formation is slow (with molecular response in minutes and the consequences being evident for hours), and strong interactions lead to enhanced biofilm formation. Unique among functional amyloids, fungal adhesin β-aggregation can be triggered by the application of physical shear force, leading to cellular responses to flow-induced stress and the formation of robust biofilms that persist under flow. Bioinformatics analysis suggests that this phenomenon may be widespread. Analysis of fungal abscesses shows the presence of surface amyloids in situ, a finding which supports the idea that phase changes to an amyloid-like state occur in vivo. The amyloid-coated fungi bind the damage-associated molecular pattern receptor serum amyloid P component, and there may be a consequential modulation of innate immune responses to the fungi. Structural data now suggest mechanisms for the force-mediated induction of the phase change. We summarize and discuss evidence that the sequences function as triggers for protein aggregation and subsequent cellular aggregation, both in vitro and in vivo.

TRANSMISSION, EVOLUTION, AND ENDOGENIZATION: LESSONS LEARNED FROM RECENT RETROVIRAL INVASIONS

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Summary: Viruses of the subfamily *Orthoretrovirinae* are defined by the ability to reverse transcribe an RNA genome into DNA that integrates into the host cell genome during the intracellular virus life cycle. Exogenous retroviruses (XRVs) are horizontally transmitted between host individuals, with disease outcome depending on interactions between the retrovirus and the host organism. When retroviruses infect germ line cells of the host, they may become endogenous retroviruses (ERVs), which are permanent elements in the host germ line that are subject to vertical transmission. These ERVs sometimes remain infectious and can themselves give rise to XRVs. This review integrates recent developments in the phylogenetic classification of retroviruses and the identification of retroviral receptors to elucidate the origins and evolution of XRVs.
and ERVs. We consider whether ERVs may recurrently pressure XRVs to shift receptor usage to sidestep ERV interference. We discuss how related retroviruses undergo alternative fates in different host lineages after endogenization, with koala retrovirus (KoRV) receiving notable interest as a recent invader of its host germ line. KoRV is heritable but also infectious, which provides insights into the early stages of germ line invasions as well as XRV generation from ERVs. The relationship of KoRV to primate and other retroviruses is placed in the context of host biogeography and the potential role of bats and rodents as vectors for interspecies viral transmission. Combining studies of extant XRVs and “fossil” endogenous retroviruses in koalas and other Australasian species has broadened our understanding of the evolution of retroviruses and host-retrovirus interactions.

Multiple Inhibitory Factors Act in the Late Phase of HIV-1 Replication: a Systematic Review of the Literature
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Summary: The use of lentiviral vectors for therapeutic purposes has shown promising results in clinical trials. The ability to produce a clinical-grade vector at high yields remains a critical issue. One possible obstacle could be cellular factors known to inhibit human immunodeficiency virus (HIV). To date, five HIV restriction factors have been identified, although it is likely that more factors are involved in the complex HIV-cell interaction. Inhibitory factors that have an adverse effect but do not abolish virus production are much less well described. Therefore, a gap exists in the knowledge of inhibitory factors acting late in the HIV life cycle (from transcription to infection of a new cell), which are relevant to the lentiviral vector production process. The objective was to review the HIV literature to identify cellular factors previously implicated as inhibitors of the late stages of lentivirus production. A search for publications was conducted on MEDLINE via the PubMed interface, using the keyword sequence “HIV restriction factor” or “HIV restriction” or “inhibit HIV” or “repress HIV” or “restrict HIV” or “suppress HIV” or “block HIV,” with a publication date up to 31 December 2016. Cited papers from the identified records were investigated, and additional database searches were performed. A total of 260 candidate inhibitory factors were identified. These factors have been identified in the literature as having a negative impact on HIV replication. This study identified hundreds of candidate inhibitory factors for which the impact of modulating their expression in lentiviral vector production could be beneficial.

Regulation of Sensing, Transportation, and Catabolism of Nitrogen Sources in Saccharomyces cerevisiae
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Summary: Nitrogen is one of the most important essential nutrient sources for biogenic activities. Regulation of nitrogen metabolism in microorganisms is complicated and elaborate. For this review, the yeast Saccharomyces cerevisiae was chosen to demonstrate the regulatory mechanism of nitrogen metabolism because of its relative clear genetic background. Current opinions on the regulation processes of nitrogen metabolism in S. cerevisiae, including nitrogen sensing, transport, and catabolism, are systematically reviewed. Two major upstream signaling pathways, the Ssy1-Ptr3-Ssy5 sensor system and the target of rapamycin pathway, which are responsible for sensing extracellular and intracellular nitrogen, respectively, are discussed. The ubiquitination of nitrogen transporters, which is the most general and efficient means for controlling nitrogen transport, is also summarized. The following metabolic step, nitrogen catabolism, is demonstrated at two levels: the transcriptional regulation process related to GATA transcriptional factors and the translational regulation process related to the
general amino acid control pathway. The interplay between nitrogen regulation and carbon regulation is also discussed. As a model system, understanding the meticulous process by which nitrogen metabolism is regulated in *S. cerevisiae* not only could facilitate research on global regulation mechanisms and yeast metabolic engineering but also could provide important insights and inspiration for future studies of other common microorganisms and higher eukaryotic cells.

**The Ontogeny of a Neutrophil: Mechanisms of Granulopoiesis and Homeostasis**

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Summary: Comprising the majority of leukocytes in humans, neutrophils are the first immune cells to respond to inflammatory or infectious etiologies and are crucial participants in the proper functioning of both innate and adaptive immune responses. From their initial appearance in the liver, thymus, and spleen at around the eighth week of human gestation to their generation in large numbers in the bone marrow at the end of term gestation, the differentiation of the pluripotent hematopoietic stem cell into a mature, segmented neutrophil is a highly controlled process where the transcriptional regulators C/EBP-α and C/EBP-δ play a vital role. Recent advances in neutrophil biology have clarified the life cycle of these cells and revealed striking differences between neonatal and adult neutrophils based on fetal maturation and environmental factors. Here we detail neutrophil ontogeny, granulopoiesis, and neutrophil homeostasis and highlight important differences between neonatal and adult neutrophil populations.