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During tetrapod evolution, the limb skeleton has undergone multiple types of modifications as part of adaptations to different modes of life and locomotion. Most strikingly, all these diverse anatomies derive from the modification of an ancestral skeletal prototype with five digits. In particular, modern artiodactyls such as pigs or cattle walk on the tip of two hoofed toes, having reduced or eliminated the rest of the digits in both fore- and hindlimbs. We have performed a comprehensive analysis of limb development in the pig (*Sus scrofa*) that shows that the progressive loss of molecular anterior-posterior (AP) polarity is a shared feature between long-diverged artiodactyl lineages. This loss of distal asymmetry is linked to the failure to upregulate the SHH receptor *Ptch1* and is accompanied by the step-wise shutdown of AER-FGF signaling during digit elongation, which provides an explanation for both the loss of the anteriormost digit and the reduction of lateral digits in the pig. Finally, open chromatin profiling of mouse and pig limb buds reveals the functional divergence of approximately one third of the regulome affecting evolutionary conserved regions in the genomic landscapes of multiple genes with essential functions during limb development, including various SHH pathway components and modulators. Our strategy establishes pig as a valuable model in evolutionary developmental biology and uncovers pervasive regulatory changes that are likely part of the molecular machinery underlying the morphological diversification of the artiodactyl limb.

S4.P.10

Impact of the expression of human CTCF protein on the S*accharomyces cerevisiae* genome

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In contrast to other eukaryotes, transcriptional regulation is particularly complex in animals, where it depends on long-range interactions between multiple distal enhancers and their target promoters. This is specially so in developmental genes, which usually have very complex expression patterns that require the control of many *cis*-regulatory elements.

Thus, 3D chromatin organization is critical to guarantee proper *cis*-regulatory interactions and to avoid spurious ones. In different groups of animals, such as humans and other vertebrates, the protein CTCF works as an essential factor to control the 3D structure of the genome, regulating cohesin-mediated chromatin interactions and the formation of loops between distal enhancers and their target promoters. In contrast, this type of long-range *cis*-regulation and its associated 3D chromatin organization have not been observed in other eukaryotic lineages such as plants and fungi. Interestingly, CTCF is also absen t from the genome of these non-animal species. To investigate how CTCF can contribute to the establishment of long-range chromatin interactions in animals, we use the model organism *Saccharomyces cerevisiae* to study the effects that CTCF expression may have on the 3D organization of a fungal genome that does not have distal *cis*-regulation. We have successfully generated a yeast strain expressing human CTCF in which we have also introduced several transgenes of human-derived boundary elements containing CTCF binding sites. Using this model we are studying the ability of CTCF to establish 3D structures on the yeast chromatin, and its potential impact on the transcriptional regulation of this unicellular species.

SESSION S5. MICROBIAL EVOLUTION

S5.P.1 Phylogenomic analysis of the zoonotic pathogen *Vibrio vulnificus*

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Vibrio vulnificus (Vv) is a multi-host pathogenic species whose geographic distribution is spreading due to global warming. The species has been classically subdivided into three biotypes (Bts) defined by phenotypic traits and host range. The three Bts are human pathogens, but only Bt2 is also a fish pathogen, a capacity that is conferred by a transferable virulence plasmid (pVvbt2). Previous work using the core genome of 80 Vv strains belonging