FEATURES

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Early Life Origins of Adult-onset Neurodegenerative Disease ALS

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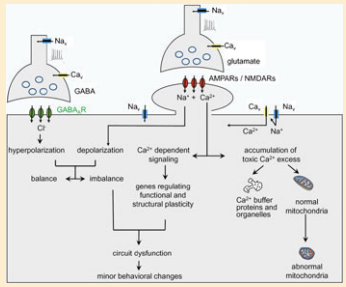

No mechanism-based cures are available for neurodegenerative disorders such as amyotrophic lateral sclerosis (ALS), Alzheimer's disease and Parkinson's disease. This is despite extensive characterization of many disease-associated mutations and the development of excellent animal models. The fact that the expression of disease-causative genes and proteins starts during embryonic stages raises the intriguing possibility that adult pathology in these devastating disorders is the result of abnormalities initiated during earlier development. Symptoms onset and disease occurs decades later only after compensatory mechanisms can no longer mask the primary insult. In favour of this idea, van Zundert et al., outline in detail pathological changes that have been detected in developing transgenic ALS mouse models expressing mutant superoxide dismutase 1 (SOD1) and discuss the changes in motor neuron physiology that occur months before the onset of behavioral symptoms. A series of critical issues are discussed highlighting the importance of determining the earliest cellular pathophysiology to identify the primary target(s) of SOD1. This effort promises to uncover novel approaches for developing pre-symptomatic diagnostic tools and for the design of new therapies that enhance the nervous system own mechanisms for protection to effectively mitigate or delay the onset of irreversible neuronal damage.

Inheritance of nuclear structure

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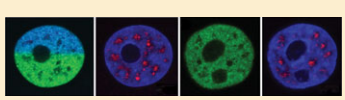

Although it is well known that chromosomes are non-randomly organized during interphase, it is not completely clear whether higher-order chromatin structure is transmitted from mother to daughter cells. Orlova et al. addresses how chromatin is rearranged during interphase and whether heterochromatin pattern is transmitted after mitosis. Additionally they tested the similarity of chromatin arrangement in sister interphase nuclei. They noticed a very active cell rotation during interphase, especially when histone hyperacetylation was induced or transcription was inhibited. This natural phenomenon can influence the analysis of nuclear arrangement. Using photoconversion of Dendra2-tagged core histone H4, Orlova et al. showed that the distribution of chromatin in daughter interphase nuclei differed from that in mother cells. Similarly, the nuclear distribution of heterochromatin protein 1b (HP1b) was not completely identical in mother and daughter cells. However, identity between mother and daughter cells was in many cases evidenced by nucleolar composition. Moreover, morphology of nucleoli, HP1b protein, Cajal bodies, chromosome territories, and gene transcripts were identical in sister cell nuclei. They conclude that the arrangement of interphase chromatin is not transmitted through mitosis, but the nuclear pattern is identical in naturally synchronized sister cells. It is also necessary to take into account the possibility that cell rotation and the degree of chromatin condensation during functionally specific cell cycle phases might influence our view of nuclear architecture

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PPAR-mediated glioblastoma therapy

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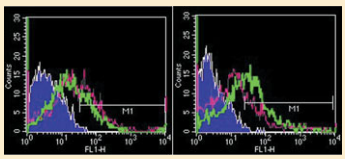

Gliobastoma (GB), the most common adult brain tumor, infiltrates normal brain area rendering impossible the complete surgical resection, resulting in a poor median survival (14–15 months), despite the aggressive multimodality treatments post-surgery, such as radiation and chemo-therapy. GB is characterized by hypoxic and necrotic regions due to a poorly organized tumor vascularization, leading to inadequate blood supply and consequently to hypoxic and necrotic areas. Under hypoxia GB primary cells increased the expression of stemness markers as well as the expression of the nuclear receptor peroxisome proliferator-activated receptor a (PPARa) and also the crucial role played by PPARs in mouse neural stem cells maintenance and differentiation. Due to the importance of lipid signaling in cell proliferation and differentiation, the expression of PPARs was analyzed in GB neurospheres both in normoxic and hypoxic conditions. The results obtained suggest a differential regulation of the three PPARs by hypoxia, thus indicating a possible therapeutic strategy to counteract GB recurrences.

Histone H2A.Z is a transcription factor ZNF24 interactor

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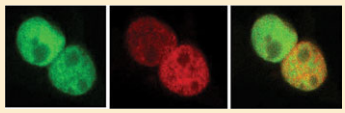

ZNF24 is a pleiotropic factor that has a role in transcription regulation, hematopoiesis, brain development, and cancers, but the molecular mechanisms underlying its functions are not clearly understood. In this study, histone variant H2A.Z has been identified in yeast-two-hybrid assays with ZNF24 as bait. GST pull-down, co-immunoprecipitation and co-localization assays confirm the interaction between ZNF24 and H2A.Z. H2A.Z has been implicated in many diverse biological processes. High expression of H2A.Z is ubiquitously detected in the progression of breast cancer, and is significantly associated with lymph node metastasis and patient survival. The results provide important information for the molecular mechanisms of ZNF24 functions and suggest that ZNF24 may be is implicated in transcriptional regulation of genes associated with oncogenesis by interaction with H2A.Z.