

Profiling trait anxiety: Transcriptome analysis reveals Cathepsin B (*Ctsb*) as a novel candidate gene for emotionality in mice

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Behavioral endophenotypes are determined by a multitude of counteracting but precisely balanced molecular and physiological mechanisms. In this study, we aim to identify potential novel molecular targets that contribute to the multigenic trait “anxiety”. We used microarrays to investigate the gene expression profiles of different brain regions within the limbic system of mice which were selectively bred for either high (HAB) or low (LAB) anxiety-related behavior, and also show signs of comorbid depression-like behavior.

We identified and confirmed sex-independent differences in the basal expression of 13 candidate genes, using tissue from the entire brain, including coronin 7 (*Coro7*), cathepsin B (*Ctsb*), muscleblind-like 1 (*Mbnl1*), metallothionein 1 (*Mt1*), solute carrier family 25 member 17 (*Slc25a17*), tribbles homolog 2 (*Trib2*), zinc finger protein 672 (*Zfp672*), syntaxin 3 (*Stx3*), ATP-binding cassette, sub-family A member 2 (*Abca2*), ectonucleotide pyrophosphatase/phosphodiesterase 5 (*Enpp5*), high mobility group nucleosomal binding domain 3 (*Hmgn3*) and pyruvate dehydrogenase beta (*Pdhb*). Additionally, we confirmed brain region-specific differences in the expression of synaptotagmin 4 (*Syt4*).

Our identification of about 90 polymorphisms in *Ctsb* suggested that this gene might play a critical role in shaping our mouse model’s behavioral endophenotypes. Indeed, the assessment of anxiety-related and depression-like behaviors of *Ctsb* knock-out mice revealed an increase in depression-like behavior in females.

Altogether, our results suggest that *Ctsb* has significant effects on emotionality, irrespective of the tested mouse strain, making it a promising target for future pharmacotherapy.

Biography

Ludwig Czibere has completed his Ph.D in biology 2009 at the Ludwig Maximilians University in Munich, and has further conducted his postdoctoral studies at the Max Planck Institute of Psychiatry, first as a Max Planck postdoctoral fellow, then as a postdoctoral scientist. His research is focused on neurogenomics and neurotranscriptomics of anxiety- and depression-like disorders. He published about 8 papers and was awarded the Ernst and Berta Scharrer Prize of the German Society of Endocrinology (DGE) in 2009.