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# 8th BenBedPhar Scientific Meeting

*Thirty years since the discovery of NRF2*

10-11 October 2024

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“NOVA Medical School Research”  
Rua Câmara Pestana 6, 1150-082  
Lisbon, Portugal

**For:** Members of the Management Committee and Work Groups of  
the COST Action CA20121



**NOVA Medical School  
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## O.24 | Bdnf-NRF2 crosstalk in depression disorder

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The World Health Organization estimates that major depressive disorder (MDD) affects over 264 million individuals globally, posing a significant public health challenge. Treatment-resistant depression (TRD) represents a severe form of MDD with poor treatment outcomes. Genetic variations are known to impact MDD treatment responses, yet genome-wide association studies have struggled to identify consistent marker alleles. Previous research has linked the Brain Derived Neurotrophic Factor (*BDNF*) genetic polymorphism with TRD. *BDNF* is essential for neuronal survival and neuroplasticity, processes influenced by antidepressant treatment, and regulated by transcription factors like Nuclear factor erythroid 2-related factor 2 (NRF2). NRF2 regulates antioxidant and anti-inflammatory responses and plays a crucial role in depression pathogenesis. NRF2 knockout mice exhibit reduced *BDNF* levels and depression-like behaviors, indicating that NRF2 activation enhances *BDNF* expression and antidepressant efficacy. The *BDNF* rs6265 (Val66Met) polymorphism is associated with variations in antidepressant response rates. Research suggests that the interaction between *BDNF* and NRF2 pathways could enhance antidepressant effectiveness. NRF2 activation, such as through the compound sulforaphane, has demonstrated rapid antidepressant effects by increasing *BDNF* expression. Lower levels of NRF2 and *BDNF* are observed in stress-induced depression models, and ketamine treatment influences NRF2-related genes. Simultaneously, there is a growing need for efficient genotyping methods, and genosensors offer a promising solution. This presentation will address the interplay between *BDNF* and NRF2 in depression, explore its relationship in antidepressant response, and present a putative genosensor for *BDNF* rs6265 (Val66Met) polymorphism identification, improving antidepressant treatment outcome.

**Funding:** This work received financial support from FCT/MCTES (UIDP/50006/2020 DOI 10.54499/UIDP/50006/2020) through national funds and the Ibero-American Program on Science and Technology CYTED (GENOPSYSEN, P222RT011).



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