

## I. Introduction

II. NRF2 as a Master Regulator of Cellular Homeostasis. Main focus on redox control and resolution of inflammation.

III. Target validation of NRF2 role in NCCDs. Autoimmune diseases, digestive and cardiovascular system diseases, respiratory, neurodegenerative, and metabolic related maladies.

IV. Animal models for investigating NCCDs: **NRF2 and its orthologues.**

- A. Warm models (*C elegans*)
- B. Insect models (*Drosophila melanogaster*)
- C. Fish models (*Zebra fish*)
- D. Mouse models (*Mus musculus*)
- E. Rat models (*Rattus norvegicus*)
- F. Genome-edited rabbit (*Oryctolagus cuniculus*). Cardiovascular disease, cystic fibrosis, ocular diseases, muscular dystrophy. *There is not a clear relation with NRF2 or its target genes, but we could summarize some data related with advances and future application to model this NCCDs.*
- G. Genetically engineered pig models (*Sus scrofa*). Cardiovascular diseases, cancers, diabetes mellitus, Alzheimer's disease, cystic fibrosis, and Duchenne muscular dystrophy
- H. Non-human primates (*Rhesus macaque*, *Macaca mulatta*, *Callithrix jacchus*). Ageing models, neurodegenerative diseases, cardiovascular disease.

Tools to analyze NRF2 activity (Pharmacological intervention, NRF2-null, KEAP1-null, NRF2 overexpression (LV, AAV-NRF2...)). We could use specific animal to illustrate different NCCDs as examples.

Conclusions and future perspectives