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eIF4E-mediated resistance to viruses: from natural variation to synthetic alleles

Jean-Luc Gallois¹, Anna Bastet^{1,2} Nathalie Glovinazzo¹ , Camille Gauffier¹, Christophe Robaglia²
¹GAFL, INRA, 84140, Montfavet, France

²Aix Marseille University, Biologie Végétale et Microbiologie Environnementales UMR 7265,
Laboratoire de Génétique et Biophysique des Plantes, Marseille F-13009, France; CNRS,
UMR 7265 Biologie Végétale et Microbiologie Environnementales, Marseille F-13009

eIF4E translation initiation factors have emerged as major susceptibility factors for RNA viruses. Natural eIF4E-based resistance alleles are found in many species and are mostly variants that maintain the translation function of the protein. eIF4E genes represent major targets for engineering viral resistance, and gene-editing technologies can be used to make up for the lack of natural resistance alleles in some crops, often by knocking out eIF4E susceptibility factors. However, we report here how redundancy among eIF4E genes can restrict the efficient use of knockout alleles in breeding. We therefore discuss how gene-editing technologies can be used to design de novo functional alleles, using knowledge about the natural evolution of eIF4E genes in different species, to drive resistance to viruses without affecting plant physiology. As a proof of concept, we show in *Arabidopsis* how such trans-species synthetic gene design allows resistance pyramiding and broad spectrum engineering of virus resistance in plants at no yield loss.

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