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**(54) Title (EN):** METHOD FOR TEMPORALLY CONTROLLING THE BIOLOGICAL ACTIVITY OF PROTEINS IN VERTEBRATES, AND APPLICATIONS THEREOF

**(54) Title (FR):** PROCÉDÉ POUR CONTRÔLER TEMPORAIREMENT L'ACTIVITÉ BIOLOGIQUE DE PROTÉINES CHEZ LES VERTÉBRÉS, ET SES APPLICATIONS

**(57) Abstract:**

**(EN):** The present invention relates to a method for tightly temporally controlling the biological activity of a protein of interest in a vertebrate, upon induction of the activity of a fusion protein comprising said protein of interest and an ERM polypeptide containing a mutated ligand binding domain of the human oestrogen receptor #, with a synthetic ligand that does not interfere with oestrogen signalling. In particular, the present invention concerns a method for generating tightly temporally-controlled targeted somatic mutations in a vertebrate, preferably a mouse, by inducing the activity of a fusion protein comprising a site-specific recombinase protein and an ERM polypeptide, with a synthetic ligand devoid of oestrogenic and anti-oestrogenic activities.

**(FR):** La présente invention concerne un procédé pour un contrôle temporaire ferme de l'activité biologique d'une protéine intéressante chez un vertébré, lors de l'induction de l'activité d'une protéine de fusion comprenant ladite protéine intéressante et un polypeptide ERM contenant un domaine de liaison au ligand muté du récepteur # des œstrogènes humains, celui-ci étant un ligand synthétique qui n'interfère pas avec la signalisation des œstrogènes. En particulier, la présente invention concerne un procédé pour générer des mutations somatiques ciblées avec un contrôle temporaire ferme chez un vertébré, de préférence une souris, en

induisant l'activité d'une protéine de fusion comprenant une protéine recombinase régio-spécifique et un polypeptide ERM, avec un ligand synthétique dépourvu des activités œstrogénique et anti-œstrogénique.

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**Declarations:**

Declaration made as applicant's entitlement, as at the international filing date, to apply for and be granted a patent (Rules 4.17(ii) and 51bis.1(a)(ii)), in a case where the declaration under Rule 4.17(iv) is not appropriate

Declaration made as applicant's entitlement, as at the international filing date, to claim the priority of the earlier application, where the applicant is not the applicant who filed the earlier application or where the applicant's name has changed since the filing of the earlier application (Rules 4.17(iii) and 51bis.1(a)(iii))