



January 16, 2019  
TRANS GENIC INC.  
(Code No.2342 TSE Mothers)

## Patent on Inflammatory Stress-Visualized Mouse has been Decided to Grant in Japan

TRANS GENIC INC. (CEO: Kenji Fukunaga, Fukuoka-shi, Fukuoka, Japan) hereby announces that, the decision to grant the patent on the production of inflammatory stress-visualized mouse and its diagnostic application has been delivered by Japan Patent Office. TRANS GENIC, National University Corporation Kumamoto University (President: Shinji Harada, Kumamoto-shi, Kumamoto, Japan, "Kumamoto University"), and National University Corporation Gunma University (President: Hiroshi Hiratsuka, Maebashi-shi, Gunma, Japan, "Gunma University") jointly filed the international patent application on this technology on July 31, 2014 (PCT/JP2014/070798).

### 【Overview】

IL-1 $\beta$  is a cytokine which is known to be associated with various diseases such as autoimmune disease, cancer, arteriosclerosis, obesity, Alzheimer's disease and aging, and draws attention as an inflammatory marker. The invention of this patent, the achievement of the joint research between Kumamoto University, Gunma University and TRANS GENIC, is related to inflammatory stress-visualized mouse that enables to detect the inflammatory response in the living body by visualizing IL-1 $\beta$  production.

This mouse model uses the new technology which can visualize the transcriptional regulation of IL-1 $\beta$  and its processing mechanism at the cellular level by luciferase (please refer to the attached document). It is expected to contribute to the understanding of the pathological mechanism of various diseases caused by inflammatory response, as well as research and development of the treatment method.

TRANS GENIC has been developing pathological condition-visualized mouse, and integrated stress response indicator mouse, endoplasmic reticulum stress<sup>※1</sup> indicator mouse, oxidative stress<sup>※2</sup> indicator mouse, and inflammation indicator mouse are already available as part of mouse model product lineup. TRANS GENIC will continuously promote the development of mouse models for various purposes.

This patent acquisition will not have a material impact on the business result or financial performance for the fiscal year 2018. TRANS GENIC will actively promote the improvement of profitability to enhance organizational performance.

#### ◆Reference: <sup>※1</sup> Endoplasmic reticulum stress

Endoplasmic reticulum is an organelle which has a role of protein production and its quality control inside the cells. Endoplasmic reticulum stress is caused by the accumulation of denatured protein (defective protein), which is considered to induce cellular death, and cause neurodegenerative diseases such as Alzheimer's disease, metabolic syndrome, and cancer.

#### <sup>※2</sup> Oxidative stress

Oxidative stress is the increased status of oxidative reaction in the body, which

causes oxidative degeneration of the biogenic substances such as DNA, lipid and protein, and leads to cellular dysfunction. These degenerated biogenic substances are considered to be the factors for arteriosclerosis, diabetes, and rheumatism.

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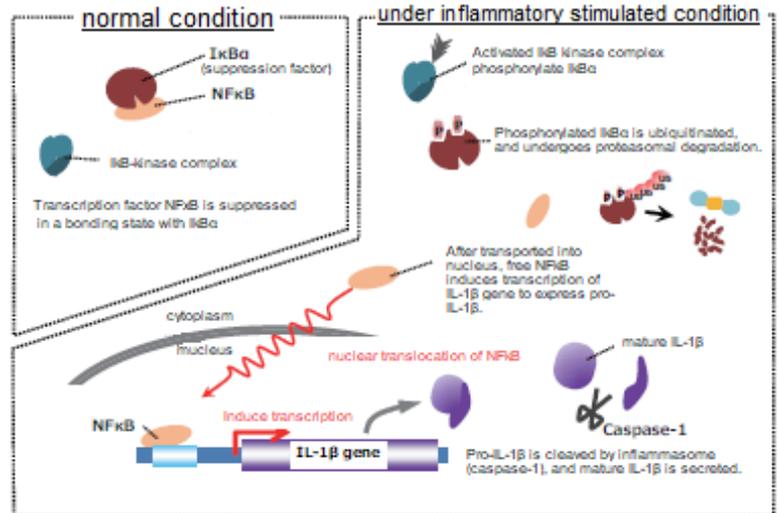
## Inflammatory response-visualized mouse: IDOL

### IL-1 $\beta$ based Dual Operating Luc

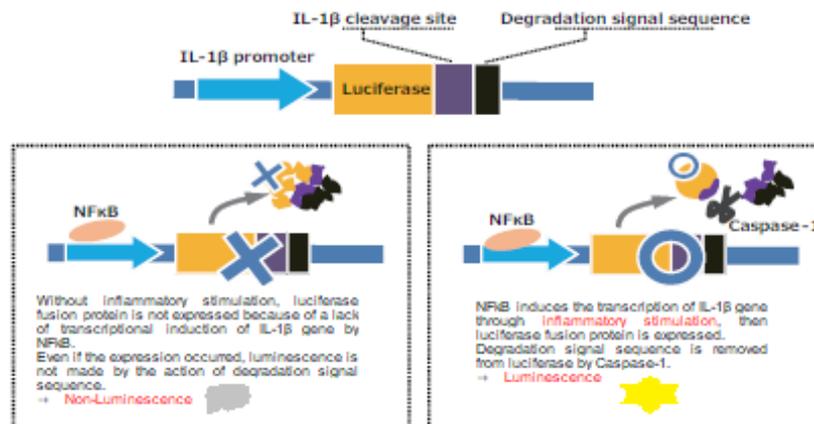
The regulation mechanism of inflammatory cytokine IL-1 $\beta$  production/ secretion

IDOL mouse is a reporter mouse model in which the regulation of an inflammatory cytokine IL-1 $\beta$  expression is visualized.

IL-1 $\beta$  expression is regulated by the transcriptional induction by NF $\kappa$ B and processing by inflammasome. This mouse model uses this mechanism as a principal.



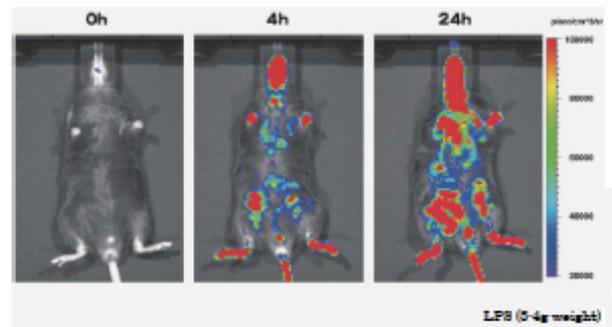
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Luminescence signal was observed throughout the whole body when Lipopolysaccharide (LPS), a substance generating systemic inflammatory response, was administered intraperitoneally.

This system is considered to be a useful tool to observe the inflammatory condition in a living body with a lapse of time.

<reference> Iwawaki *et al.* "Transgenic mouse model for imaging of interleukin-1 $\beta$ -related inflammation in vivo" *Sci. Rep.*, vol. 5, 17205, 2015.



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