“ Modified NAGA ”
～ Non-immune reaction to Fabry patients ～

【 Summary 】

***Objective*:**
To establish a new therapy for Fabry disease, we aimed to develop a novel enzyme “Modified α-N-acetylgalactosaminidase (Mod. NAGA)”, which shows higher stability and incorporation efficacy, and reduces immune reaction.

***Developed Enzyme*:**
Mod. NAGA has altered substrate specificity towards the α-galactosidase A (GLA) substrate [Fig.1]. Mod. NAGA has GLA activity and shows significant effects on Fabry mice.

***Properties and Effects*:**

1) Mod. NAGA has more mannose 6-phosphate residues compared to GLA, which increases the stability and incorporation into cells.
[Detailed data available on your request]

2) The immunological study revealed that there was no immunological cross-reactivity between Mod. NAGA and GLA. Mod. NAGA does not react to serum from Fabry patients repeated administration of recombinant GLA [Fig.2] .

3) The recurrent injections of Mod. NAGA to Fabry mice did not show any obvious changes nor produce any anti-Mod. NAGA IgG1.
[Detailed data available on your request]

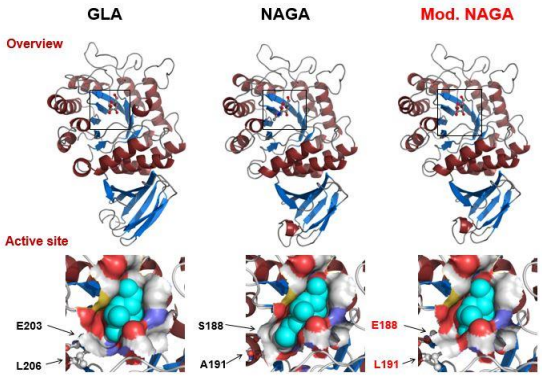
4) The administration of Mod. NAGA decreased Gb3 and Lyso-Gb3 in the liver, kidneys, and heart in Fabry mice (human NAGA-Tg-Fabry mice) [Fig.3], and pathologically improved in these organs.
[Detailed data available on your request]

【 Conclusions 】

- Mod. NAGA is a **highly promising novel enzyme** for the treatment of Fabry disease.
- Mod. NAGA can be applied not only for **ERT** but for **Cell Therapy** using iPS cells.

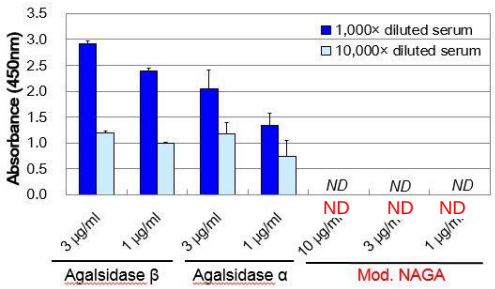
【 Properties and Effects 】

Fig. 1 Molecular Designing of Mod. NAGA



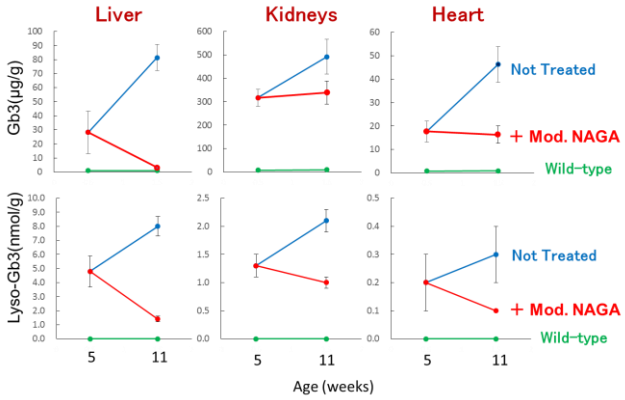
GLA and NAGA have similar 3D-structure but different substrate–recognition. Mod. NAGA was developed by two amino acids modifications: Ser188Glu and Ala191Leu, which are responsible for NAGA substrate binding. This modification does not alter the surface structure but gives GLA activity.

Fig. 2 Mod. NAGA does not induce Immune Reaction to Fabry Serum



ELISA was performed using serum from Fabry patients with repeated injection of agalsidase β.

Fig. 3 Mod. NAGA decreased Gb3 and Lyso-Gb3 in hNAGA-Tg-Fabry Mice



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【 Reference 】

Use of a Modified α-N-Acetylgalactosaminidase in the Development of Enzyme Replacement Therapy for Fabry Disease,
Y Tajima, H Sakuraba, et.al.,
Am J Hum Genet, 85, 569–580, 2009

【 Patents 】

1. NOVEL HIGHLY FUNCTIONAL ENZYME HAVING MODIFIED SUBSTRATE-SPECIFICITY, PCT/JP2006/323509, Patented at JP, US, DE, GB, FR, ES, IT, IL, and TW
2. PHARMACEUTICAL COMPOSITION FOR ENZYME REPLACEMENT THERAPY, PCT/JP2008/059604, Patented at JP, US, DE, GB, FR, ES, and IT

【Partner We Hope】

- We are looking for a company that is interested in developing a novel **ERT** and/or **Cell Therapy** for the treatment of Fabry disease.
- We can conditionally provide **more detailed data**.

【 Contact 】

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