CXCL14 inhibitors

—as drug candidates to ameliorate obesity-associated TYPE-2 DIABETES—

Summary

Our inventors aim to develop a treatment for type II diabetes by targeting CXCL14. To date, they have succeeded in developing a CXCL14 knockout mouse and an anti-human CXCL14 monoclonal antibody. Recently, they have identified the CXCL14 receptors and developing CXCL14 antagonistic peptides.

Advantages

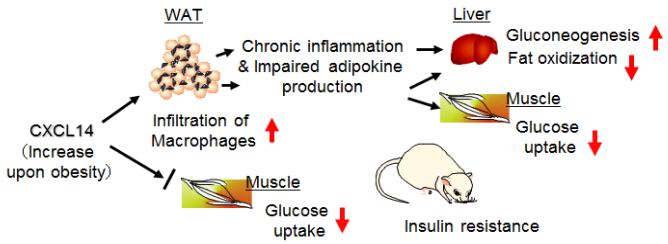
1. Establishment of CXCL14-knockout mouse strain.

(Independent of the previous knockout strain from the Moser laboratory.)

- No insulin resistance associated with obesity was observed.
- CXCL14 may play an important role in the regulation of feeding behavior in the central nervous system.

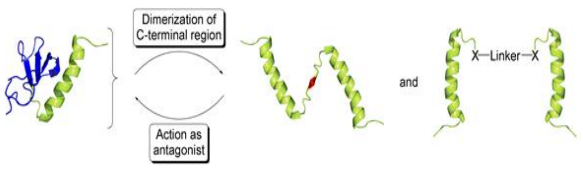
2. Identification of CXCL14 receptors and Development of CXCL14 receptor Antagonistic Peptide.

- Identified molecular components of CXCL14 receptors which contributed to revealing CXCL14 functions.
- Synthesized 30 different CXCL14 peptides and identified two peptides with inhibitory activity.



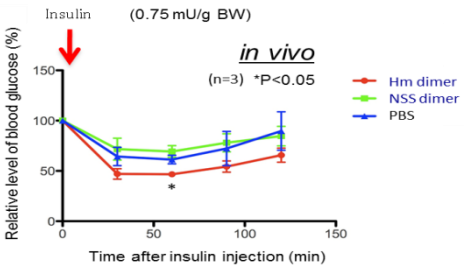
(Nara *et al.*, J. Biol. Chem., 282: 30794-30803, 2007)

CXCL14 is a risk factor for the obesity-induced type-2 diabetes.



Dimerized CXCL14 C-terminal region showed antagonistic activity.

(Tsuji *et al., 8th AFMC International Medicinal Chemistry Symposium.* **2011**.*11.30-12.2, Tokyo.*)



Hm dimer was effective for amelioration resistance in obese mice.

Proposal

Interested in the supply of CXCL14-knockout mouse strain and CXCL14 antagonist peptide?
Or interested in the collaboration with our laboratory?

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CXCL14inhibitors

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Publications

N. Nara, Y. Nakayama, (8 authors), H. Yonekawa, Y. Minokoshi, and T. Hara, *J. Biol. Chem., 282: 30794-30803,* 2007.

K. Tanegashima, K. Suzuki, Y. Nakayama, and T. Hara, *Exp. Cell Res., 316: 1263-1270,* 2010.

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K. Tsuji, K. Tanegashima, (4 authors), T. Hara, and A. Otaka, *8th AFMC International Medicinal Chemistry Symposium "Frontier of Medicinal Science". 2011.11.30-12.2, Tokyo.*

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K. Tanegashima, (5 authors), T. Hara, FEBS Letters, 587: 1731-1735, 2013.

K. Tanegashima, (4 authors), T. Hara, FEBS Letters, published online 23 October 2013. (http://www.febsletters.org/article/S0014-5793(13)00774-6/abstract)

Inventors

1. Establishment of CXCL14-knockout mouse strain.

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2. Identification of CXCL14 receptors and Development of CXCL14 receptor Antagonistic Peptide.

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Patent

1. PCT / JP2006 / 324622
2. Under application in JAPAN

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