構造解析ユニット

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濡木　理（東京大学大学院 理学系研究科・教授）

高難度膜タンパク質等の調製と構造解析可能なグリッド調製の支援

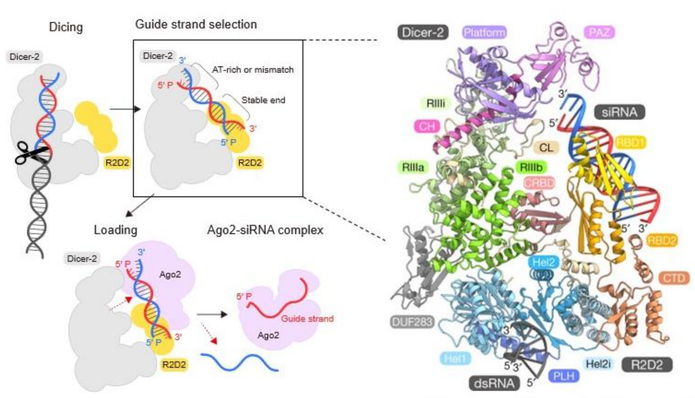
補助事業分担者（所属・職名）
木瀬　孔明（東京大学 大学院理学系研究科・特任准教授）、志甫谷　渉（東京大学 大学院理学系研究科・助教、現在・慶應義塾大学 医学部・准教授）、
石谷　隆一郎（東京科学大学 難治疾患研究所・教授）

支援の成果：高難度タンパク質とグリッドの調製支援とGlaciosによるグリッドスクリーニングの支援

R2D2によるsiRNA末端の認識とAgo2への受け渡し機構

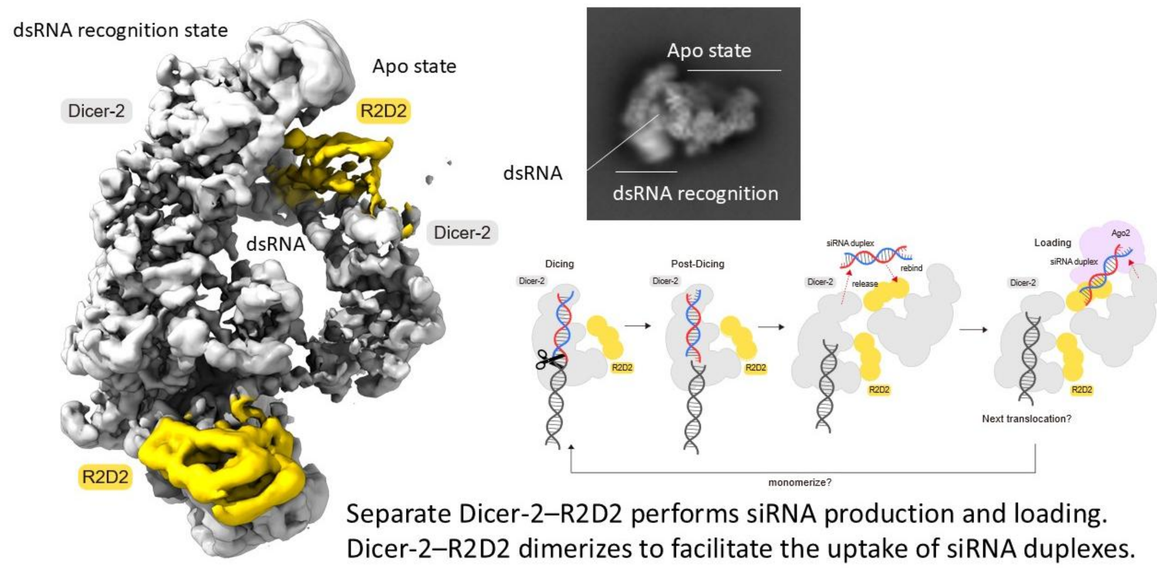


東京大学定量研
泊 幸秀 教授
の支援



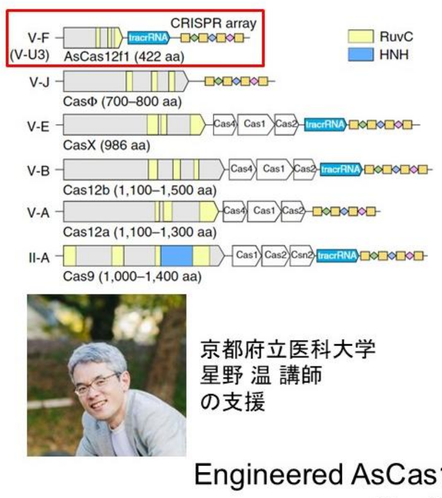
Yamaguchi et al., Nature, 2022

Ago2 binds to guide siRNAs and suppresses viral RNAs and transposons
Dicer-2-R2D2 is involved in substrate cleavage and guide strand selection
→How Dicer-2-R2D2 advances two roles?

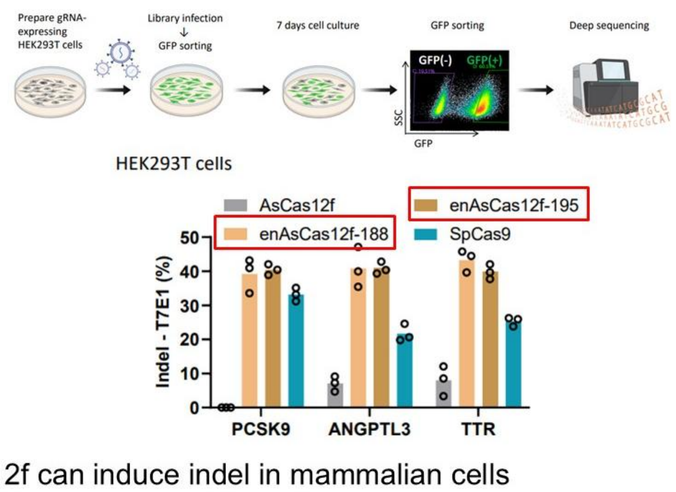


Separate Dicer-2–R2D2 performs siRNA production and loading.
Dicer-2–R2D2 dimerizes to facilitate the uptake of siRNA duplexes.

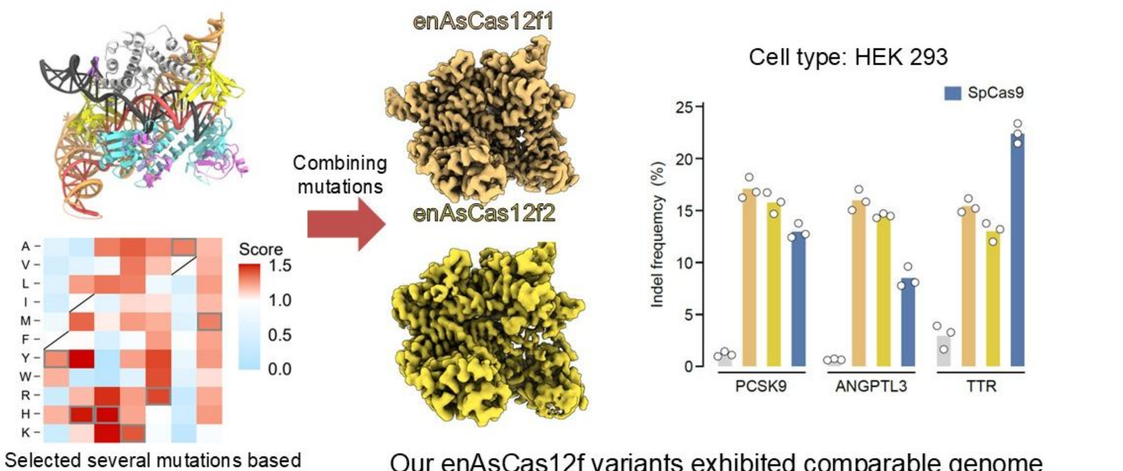
AsCas12fの構造基盤と合成生物学的手法に基づいた高活性ゲノム編集ツールの開発



京都府立医科大学
星野 温 講師
の支援



Engineered AsCas12f can induce indel in mammalian cells
with efficiency comparable to Cas9
→Molecular mechanism is unknown



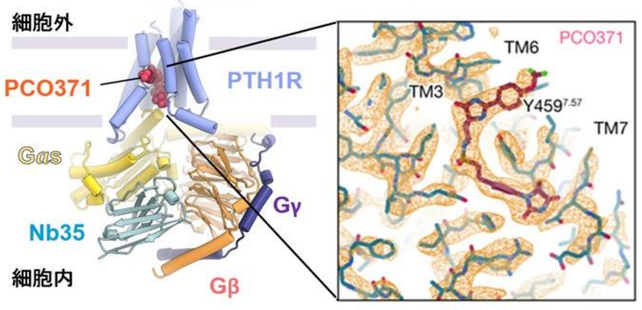
Our enAsCas12f variants exhibited comparable genome editing activities in human cells to those of SpCas9

Hino *et* al., Cell, 2023

PCO371によるPTH1Rの新規Gタンパク質選択的活性化機構

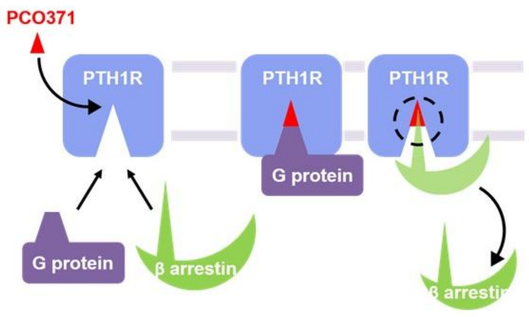


京都大学
井上 飛鳥 教授
の支援

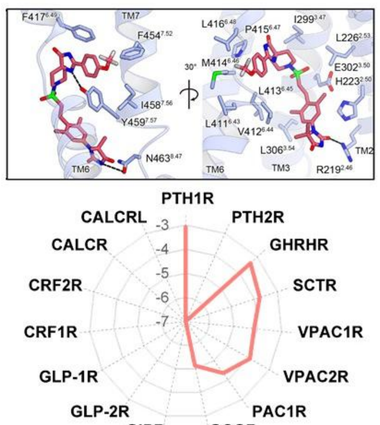


(Kobayashi *et al.*, *Nature*, 2023)

PCO371 directly links PTH1R to G proteins, but not β-arrestins.



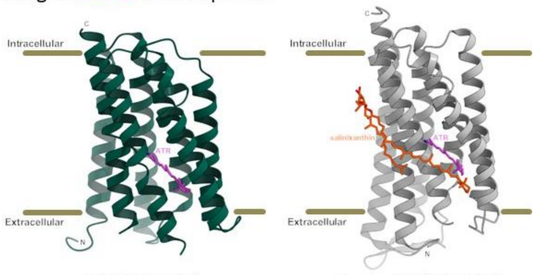
PCO371 activates nearly half of class B1 GPCRs.



(Kobayashi *et al.*, *Nature*, 2023)

カロテノイドを発色団として持つ新規光駆動型プロトンポンプ Kin4B8 の光エネルギー利用構造基盤

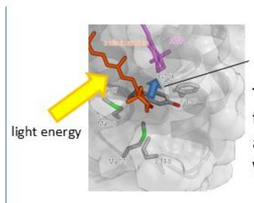
Common rhodopsin is activated by absorbing light energy using its retinal chromophore.



GPR (PDB:7B03)　　*S. ruber* XR (PDB:3DDL)

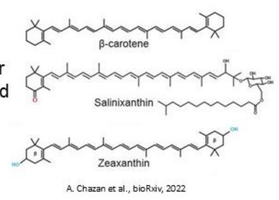
On the other hand, energy transfer from ketocarotenoids to light-driven proton pumps has been demonstrated.

Rhodopsins contain ketocarotenoids as an antenna can harvest an additional 50% energy compared to antenna-less rhodopsins.



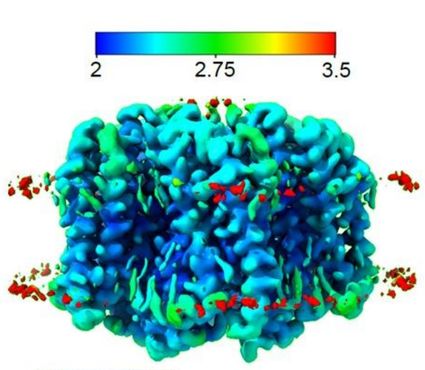
The ring moiety of salinixanthin fits into the fenestration in *s. ruber* XR and forms van der Waals interactions with the retinal β-ionone ring

We detected light energy transfer from the widespread hydroxylated carotenoid zeaxanthin to the retinal moiety of XRs



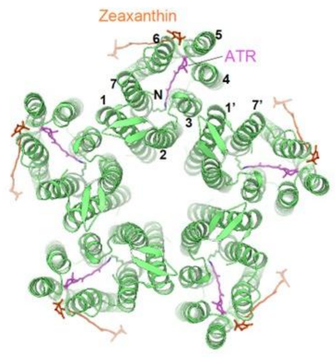
A. Chazan et al., bioRxiv, 2022

To examine such hydroxylated carotenoids binding to XRs, we determined the cryo-EM structure of Kin4B8, a member of the XR family, with zeaxanthin.



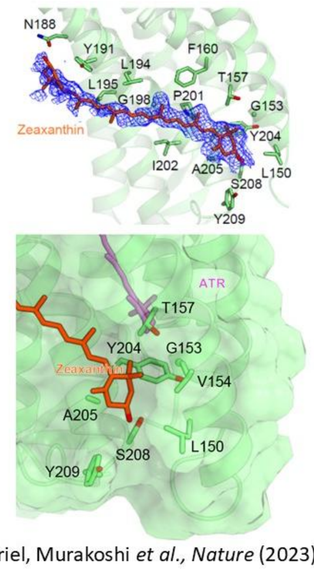


名古屋工業大学
神取 秀樹 教授の支援



The structure of Kin4B8 with zeaxanthin determined as a pentamer.

Zeaxanthin binding to Kin4B8 from the outside of the structure was successfully observed at a high resolution of 2.33 Å.



Ariel, Murakoshi *et al., Nature* (2023)

COIの開示：本発表に関して、開示すべき利益相反（COI）はありません