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# Family tuntun ti RNA-guided DNA-targeting systems — yàtọ̀ sí CRISPR, kò sì tíì jẹ́ gene-editing tool

*Nípa mining microbial genomes pẹ̀lú protein structures, researchers rí TIGR-Tas, family tuntun ti RNA-guided systems tí ń cut DNA pẹ̀lú two-part guide àti láìní "PAM" landing site. Wọ́n fi hàn pé version kan programmable nínú human cells, ṣùgbọ́n efficiency kéré, wọ́n sì trace deep evolutionary links sí RNA-guided machines mìíràn. Real expansion ti RNA-guided biology ni, possible starting point fún future tools — basic-science discovery àti proof of concept, kì í ṣe mature editor tàbí therapy.*

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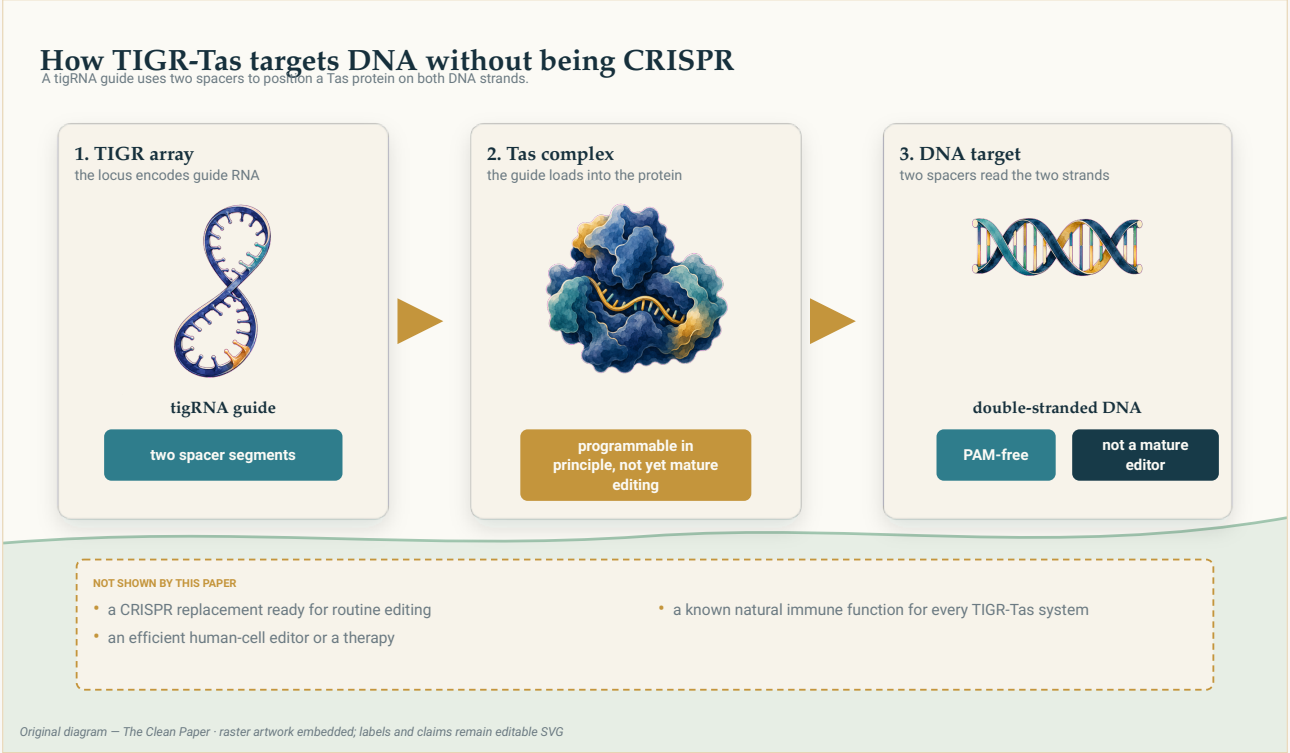
# Ẹ̀ka tuntun kan lórí igi àwọn RNA-guided machines

Nígbà díẹ̀, biology ìwé ìwádìí kan máa ń dé pẹ̀lú àkọlé tí kò béèrè fún. Tí èyí gba ni “CRISPR tuntun kan.” Iṣẹ́ tó wà lẹ́yìn rẹ̀ fanimọ́ra ju bẹ́ẹ̀ lọ — ó sì tún dín síi, bí ó ṣe sábà rí.

Ẹ jẹ́ ká bẹ̀rẹ̀ pẹ̀lú ohun tí CRISPR mú di olókìkí: **RNA-guided ètò**. Ẹ̀tan náà ni pé prótínì kò nílò kí a hard-wire rẹ̀ láti recognize target kan. Dípò bẹ́ẹ̀, ó gbe short piece of RNA — guide kan — ó sì lọ sí ibi tí sequence guide náà bá match. Yí guide padà, target náà yí. Programmability yìí ni ìdí tí CRISPR fi di irinṣẹ́. Ṣùgbọ́n CRISPR kì í ṣe RNA-guided ètò kan ṣoṣo nínú nature, ìbéèrè ìwé ìwádìí yìí sì jẹ́ èyí tó ní sùúrù: irú ètò *mìíràn* mélòó ni wà, kí ni wọ́n lè kọ́ wa?




TIGR-Tas lo guide tí ó ní spacers méjì láti ka opposite strands ti DNA. Architecture tuntun ni, kì í ṣe ready-made jíní editor.



Láti wá wọn, òǹkọ̀wé kò search fún matching jíní sequences — wọ́n máa ń yí púpọ̀ kọjá evolutionary àkókò, nítorí náà distant relatives lè ṣọnù. Wọ́n search fún *shapes*. Wọ́n bẹ̀rẹ̀ láti apá CRISPR Cas9 prótínì tí ó di guide RNA mú, wọ́n sì wá predicted prótínì ìṣètò databases fún ohun tí a kọ́ ní ọ̀nà kan náà. Trail yẹn lọ — nípasẹ̀ bacterial “jumping jíní” kan àti machinery tí ordinary seẹli ń lò láti chemically tweak RNA ara wọn — sí ohun tuntun gidi.

## Ohun tí àwọn olùkọ̀wé ṣe

Structural search náà rí previously unrecognised family of prótínì, tí a encode púpọ̀ jù lọ nínú bacteriophages (viruses tí ń infect bacteria), viruses of archaea, àti tiny parasitic bacteria. Ọkọọkan wà légbẹ̀ẹ́ distinctive stretch

of DNA: long repeating array tí òǹkọ̀wé pe ní **TIGR array** (Tandem Interspaced Guide RNA). Wọ́n pe prótínì náà ní **Tas** (TIGR-associated). Díẹ̀ Tas prótínì jẹ́ bare RNA-gripping part nìkan; àwọn mìíràn ní DNA-cutting irinṣẹ́ — ọkan nínú molecular scissors méjì (RuvC tàbí HNH) — tí a so mọ́ wọn.

Lẹ́yìn tí wọ́n rí family náà nínú database, wọ́n gbe e wọ lab: wọ́n express èto náà nínú *E. coli*, wọ́n sequence small RNAs tí wọ́n ṣe, wọ́n mọ òfin tí RNAs yẹn fi ń rí DNA target, wọ́n ìdánwò bóyá cutting versions ń cut gan-an, wọ́n gbìyànjú láti program ọkan fún editing ènìyàn sẹ̀li, nikẹhin wọ́n freeze working complex kan wọ́n sì image ìṣètò rẹ̀ ní near-atomic resolution.

# Ohun tí wọ́n rí

**Guide náà wà ní apá méjì.** TIGR array ni a ìlànà sí short RNAs tó ní nípa 36 letters, ọkọ̀ọkan ní *targeting segments méjì* tó yàtọ̀. Segment kan ka strand kan ti target DNA; omiì ka opposite strand. Mejeeji ṣiṣẹ́ pọ̀ láti pin site kan mọ́. Èyí jẹ́ mechanistic departure gidi láti CRISPR, tí guide rẹ̀ ń match single strand nínú continuous stretch kan.

**Kò sì nílò "landing pad."** Ọ̀pọ̀ CRISPR nucleases lè cut nìkan ní lẹ́gbẹ̀ẹ́ short specific DNA motif ("PAM") tó wà beside target — constraint tó ń àálà ibi tí wọ́n lè aim. TIGR èto kò fi requirement bẹ́ẹ̀ hàn: target sequence funra rẹ̀ ni wọ́n gbára lé. System tí kò nílò PAM lè, ní principle, target sí i places.

**Cutting versions náà cut precisely.** Pẹ̀lú little RNA guide, RuvC- àti HNH-bearing Tas prótínì ṣe clean, sequence-specific breaks nínú DNA — wọn kò sì ṣe nǹkan láìsí guide.

**ẹ̀dà kan lè program fún editing ènìyàn sẹ̀li — ṣùgbọ́n barely.** Nígbà tí a gbe wọ ènìyàn sẹ̀li nínú dish, a sì aim sí jínì méfà, Tas prótínì kan ṣe edits, tó confirm pé èto programmable nínú sẹ̀li wa. Ṣùgbọ́n efficiency kéré: best ọ̀ràn jẹ́ few percent of sẹ̀li. Fún ìfiwéra, today's optimized CRISPR irinṣẹ́ routinely edit large fraction of sẹ̀li. Èyí jẹ́ proof pé ó *lè* ṣiṣẹ́, kì í ṣe irinṣẹ́ tí ń ṣiṣẹ́ *dáadáa*.

**Structure ṣàlàyé ọ̀nà iṣẹ́ — ó sì hint origins rẹ̀.** Imaged complex jẹ́ mirror-symmetric pair of prótínì tí ó clasp figure-eight-shaped guide RNA, pẹ̀lú target DNA tí a bend sharply. Strikingly, architecture náà jọ machine kan nínú relatives ti sẹ̀li wa — box C/D **snoRNP**, tí ó guide chemical edits sí RNA dípò kó cut DNA.

**Natural job rẹ̀ kò dájú.** Nígbà òǹkọ̀wé express èto kan nínú *E. coli*, kò *fend off* invading viruses tàbí plasmids — day job ti CRISPR. Dípò bẹ́ẹ̀ ó gradually purge targeted plasmid kọjá generations púpọ̀, tó hint pé gidi role rẹ̀ lè wà nínú slow competition láàárín mobile DNA pieces dípò frontline immune defence. Ṣùgbọ́n artificial borrowed setting ni, honest answer ni pé a kò tíì mọ ohun tí èto wọ̀nyí ṣe nínú wild.

# Ohun tí èyí likely túmọ̀ sí

Nǹkan méjì, pẹ̀lú ìpele of ìgbẹ́kẹ̀lé tó yàtọ̀.

Solid ọkan: known world of RNA-guided èto tóbi, ó sì varied ju CRISPR àti recently rí cousins rẹ̀ lọ. TIGR-Tas jẹ́ branch tuntun gidi, pẹ̀lú own two-part, PAM-free way of recognizing DNA. Èyí jẹ́ gidi addition sí map.

Deeper, sí i speculative ọkan: nítorí TIGR machinery jẹ́ built bí snoRNP tí ń edit RNA nínú sẹ̀li bí tiwa, àti bí

known jumping jínì kan, ó lè mark evolutionary link láàárín RNA-guided *RNA*-modifying ètò àti RNA-guided *DNA*-targeting ètò — ṣeé ṣe missing piece nínú ìtàn bí programmable RNA guides ṣe arise kọjá life.

# Ohun tí èyí kò fi ẹ̀rí múlẹ̀

- Kì í ṣe **ready gene-editing irinṣẹ́**. Editing nínú èníyàn ṣẹ̀ẹ̀li hàn, ṣùgbọ́n weak — few percent best ọ̀ràn. Proof of programmability ni, kì í ṣe mature editor, ó sì jìn sí ìṣègùn lò.
- Kì í ṣe **"CRISPR 2.0."** Bí irinṣẹ́ lónìí, CRISPR-Cas9 out-edits rẹ̀ ní púpọ̀. TIGR-Tas jẹ́ tuntun *architecture* ní proof-of-concept stage, kì í ṣe better èdà of existing product.
- **Biological role rẹ̀ unknown.** Kò act bí anti-virus immune ètò nínú ọ̀kan ìdánwò; "tuntun bacterial immune ètò" kò established.
- Ọ̀pọ̀ **basic ọ̀nà iṣẹ́ ṣì open** — pẹ̀lú bí guide RNA ṣe cut sí final length àti ohun tí ètò target nínú nature (ọ̀pọ̀ wà nínú microbes tí ó nira láti culture).
- **Kò sí therapy níhìn-ín.** Discovery àti characterization nínú microbes àti ṣẹ̀ẹ̀li culture ni — no disease, no ìtọ́ju, no aláìsàn.

# Báwo ni ẹ̀rí ṣe lágbára tó?

Discovery funra rẹ̀ dúró lórí ground tó firm, ó sì well-rounded: large-scale structural mining, lab confirmation ti bí RNA ṣe form àti bí ó ṣe rí/cut DNA, near-atomic ìṣètò of complex in action, plus human-cell ìdánwò. Claim pé "tuntun distinct RNA-guided DNA-targeting family ni" well supported láti ìtọ́ṣọ́nà púpọ̀.

Ohun tó *early* ni usefulness. Editing works barely, gbogbo optimization tí yí CRISPR láti curiosity sí irinṣẹ́ ṣì wà níwájú fún TIGR. Ohun tó *inferential* ni rest of ìtàn — natural role jẹ́ reasonable guess láti artificial ìdánwò, evolutionary link jẹ́ elegant argument láti shared ìṣètò, kì í ṣe settled history. ìwé ìwádìí ṣọ́ra nípa which is which.

# Kí nìdí tí ó fi ṣe pàtàkì?

Several widenings ti RNA-guided catalogue ṣáájú ti pay off níkẹyìn. Systems lẹ́yìn today's irinṣẹ́ — Cas9, Cas12, Cas13, àti recently smaller IscB/OMEGA prótínì àti eukaryotic Fanzors — jẹ́, ní ìbẹ̀rẹ̀, newly described biology nìkan. Kò sí ọkan tó dé bí finished irinṣẹ́. System pẹ̀lú two-part guide àti no PAM requirement jẹ́ genuinely yàtọ̀ starting kókó, PAM-free targeting sì jẹ́ flexibility tí tool-builders fẹ́.

Ṣùgbọ́n quieter èsì lè ṣe pàtàkì jù irinṣẹ́ prospect. Nípa tying DNA-cutting ètò sí RNA-editing snoRNP machinery àti jumping jínì, iṣẹ́ yìí sketch ṣeé ṣe thread tó connect very yàtọ̀ RNA-guided ètò kọjá tree of life. Irú àwárí bẹ́ẹ̀ lè reorganize bí field ṣe lóye origin irinṣẹ́ rẹ̀ — tó lè ní iye púpọ̀ ju àkọlé míì nípa scissors lọ ní long run.

# Àkótán kedere

Nípa search fún prótínì *shapes* dípò sequences, olùwádìí discover TIGR-Tas: previously unknown family of RNA-guided DNA-targeting ètò, mostly nínú bacterial viruses àti parasitic bacteria. Guide RNA rẹ̀ unusual — nípa 36 letters pẹ̀lú targeting segments méjì tí ń ka opposite strands of DNA — àti unlike CRISPR, kò nílò adjacent “PAM” motif. DNA-cutting members cut precisely, ọkan lè program fún human-cell editing (ṣùgbọ́n efficiency few percent nìkan), near-atomic ìṣètò sì fi complex tó jọ snoRNP machinery tí ń edit RNA nínú sẹ̀li wa hàn — suggesting deep evolutionary link láàárín RNA-guided RNA-modifying àti DNA-targeting ètò. Èyí jẹ́ gidi expansion ti RNA-guided biology àti ṣeé ṣe chassis fún future irinṣẹ́ — basic-science discovery àti proof of concept, **kì í ṣe** mature jínì editor, kì í ṣe “CRISPR 2.0,” kì í ṣe therapy. Natural job rẹ̀ nínú wild ṣì unknown.

# Àyẹ̀wò láìsí àṣejù

**Ohun tí ìwé ìwádìí fi hàn:** New distinct RNA-guided DNA-targeting family (TIGR-Tas) nínú prokaryotes àti viruses wọn; two-segment PAM-free guide RNA (~36 nt) tó target DNA strands méjì; precise RNA-guided cleavage; programmable low-efficiency human-cell editing; near-atomic cryo-EM ìṣètò; structural/evolutionary links sí box C/D snoRNPs àti IS110 transposons.

**Ohun tó ṣeé gbà ṣùgbọ́n unproven:** Natural biological role; proposed evolutionary bridge láàárín RNA-modifying àti DNA-targeting ètò.

**Ohun tí kò fi hàn:** Mature/high-efficiency editor; superiority sí CRISPR; confirmed natural function; guide-RNA maturation ọ̀nà iṣẹ́; therapeutic application.

**Main limitations:** Human-cell editing efficiency low; most ètò live nínú hard-to-study metagenomes; biological-role àti evolutionary-origin claims inferential; characterization nínú microbes/sẹ̀li culture, kì í ṣe disease context.

**Ìgbẹ́kẹ̀lé wo ni olùkà gbogboogbo yẹ kí ó ní?** Gíga pé èyí jẹ́ genuine distinct family pẹ̀lú novel two-part PAM-free ọ̀nà iṣẹ́. Gíga pé **kì í ṣe** ready gene-editing irinṣẹ́, “CRISPR 2.0” tàbí therapy. Kéré lórí natural role àti how far it yóò go as a irinṣẹ́. Stance tó yẹ: excitement nípa tuntun biology, patience nípa applications.

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## Àwọn orísun

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