

# User Guide

Version 1.2

2022/8/12

# Contents

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<b>1</b>	<b>Introduction</b>	<b>2</b>
<b>2</b>	<b>Querying the Database</b>	<b>3</b>
<b>2.1</b>	<b>Search of information of Model</b>	<b>3</b>
<b>2.2</b>	<b>Search for RNA motif</b>	<b>8</b>
<b>3</b>	<b>Interaction</b>	<b>10</b>
<b>4</b>	<b>Statistics</b>	<b>12</b>
<b>5</b>	<b>Contact Us</b>	<b>14</b>

# 1 Introduction

RNAapt3D contains RNA sequences, their secondary/tertiary structural information, target proteins of RNA aptamers and network of RNA-protein interaction. The tertiary structures are predicted by a given RNA sequence considering a wide variety of secondary structures. This database can be used to provide insights for tertiary structural analysis, motif search with base flip position and a starting point by RNA-protein complex molecular simulations. RNAapt3D lets you creatively promote on your project for the development of new RNA aptamer.



## 2 Querying the Database

### 2.1 Search of information of Model

Menu items are shown at the top of RNAapt3D page.



#### A) Browser aptamer models

Click on the “Model” at the top menu, you can browser the RNA sequence, the target protein, and the structural information of each entry (monad’s ID).

monad ID	Sequence	Length	Target	Structure String	Secondary Structure	Tertiary Structure
<u>monad0015</u>	CAGGCUACGGUAGAGCAUCAUG AUCCUG	29	<u>PDGF- B(P01127)</u>	.....(((.....))..... ..... (((((((.....))..... ..)))) (((((((.....)).....(..... ).)))) (((((((.....)).....(((..... )))))) ..... .....		<a href="#">Model</a> <a href="#">Na+</a> <a href="#">Ont_Model</a> <a href="#">Mod_Model</a>
						<a href="#">Model</a> <a href="#">Na+</a> <a href="#">Ont_Model</a> <a href="#">Mod_Model</a>
						<a href="#">Model</a> <a href="#">Na+</a> <a href="#">Ont_Model</a> <a href="#">Mod_Model</a>
						<a href="#">Model</a> <a href="#">Na+</a> <a href="#">Ont_Model</a> <a href="#">Mod_Model</a>

## B) View detail information of RNA aptamer

Click on the “monad’s ID” (for example: monad0015) in the list, the detail of its RNA aptamer will be shown.

### Detail of monad0015

#### Aptamer Detail

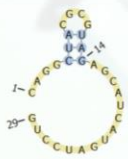
monad ID	Length	Target Molecule	Remark
monad0015	29	<a href="#">PDGF-B (P01127)</a>	Fovista is a new drug expected as a remedy for neovascular age-related macular degeneration. Currently, 3 kinds of tests shown below has been initiated. - a phase IIb randomized, double-masked, controlled trial to establish the safety and efficacy of intravitreal administration of Fovista administered in combination with Avastin compared to Avastin monotherapy in subjects with subfoveal neovascular age-related macular degeneration. - a phase III randomized, double-masked, controlled trial to establish the safety and efficacy of intravitreal administration of Fovista (Anti PDGF-B pegylated aptamer) administered in combination with either Avastin or Eylea compared to Avastin or Eylea monotherapy in subjects with subfoveal neovascular age-related macular degeneration - a phase III randomized, double-masked, controlled trial in order to establish the safety and effectiveness of intravitreal administration with combination of Fovista and Lucentis compared with administration of only Lucentis

**Sequence**  
CAGGCUACGCGUAGAGCAUCAUGAUCCUG

**Adaptation Disease**  
subfoveal neovascular age-related macular degeneration

**Product Name**      **Phase**  
Fovista                      III

#### Structure monad0015-1

Parameter	Secondary Structure
CentroidFold: CONTRAFold 2*1	
Structure String .....(((.....))).....	
Flip Position *****	
Tertiary Structure	

[Rascal Model](#)  [Na\\*](#)  [Optimized Model](#)  [Modified Model](#)  **Download**

Tertiary structure model PDB file can be downloaded by clicking icons beside model links.

## C) Inspect target protein

Click on the “Target protein’s name” (for example: PDGF-B) in the list, then Uniprot page related to its protein will open in new window. Confirm the detail of its protein.

The screenshot displays the UniProtKB entry for Platelet-derived growth factor subunit B (PDGF-B, P01127). The page is organized into several sections:

- Entry:** Protein: Platelet-derived growth factor subunit B; Gene: PDGF-B; Organism: *Homo sapiens (Human)*; Status: Reviewed - Annotation score: 5 - Experimental evidence at protein level<sup>1</sup>.
- Function:** Growth factor that plays an essential role in the regulation of embryonic development, cell proliferation, cell migration, survival and chemotaxis. Potent mitogen for cells of mesenchymal origin (PubMed:26599395). Required for normal proliferation and recruitment of pericytes and vascular smooth muscle cells in the central nervous system, skin, lung, heart and placenta. Required for normal blood vessel development, and for normal development of kidney glomeruli. Plays an important role in wound healing. Signaling is modulated by the formation of heterodimers with PDGFA (By similarity).
- Sites:** A table listing two sites involved in receptor binding.
- GO - Molecular function:** chemoattractant activity, collagen binding, and growth factor activity.

Feature key	Position(s)	Description	Actions	Graphical view	Length
Site <sup>1</sup>	108	Involved in receptor binding			1
Site <sup>1</sup>	111	Involved in receptor binding			1

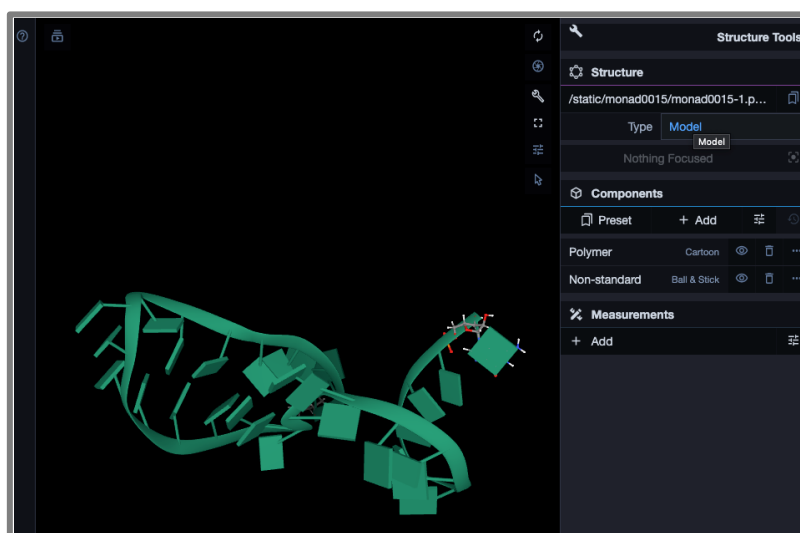
GO - Molecular function <sup>1</sup>	Source
chemoattractant activity	BHF-UCL
collagen binding	MGI
growth factor activity	UniProtKB

## D) View tertiary structure

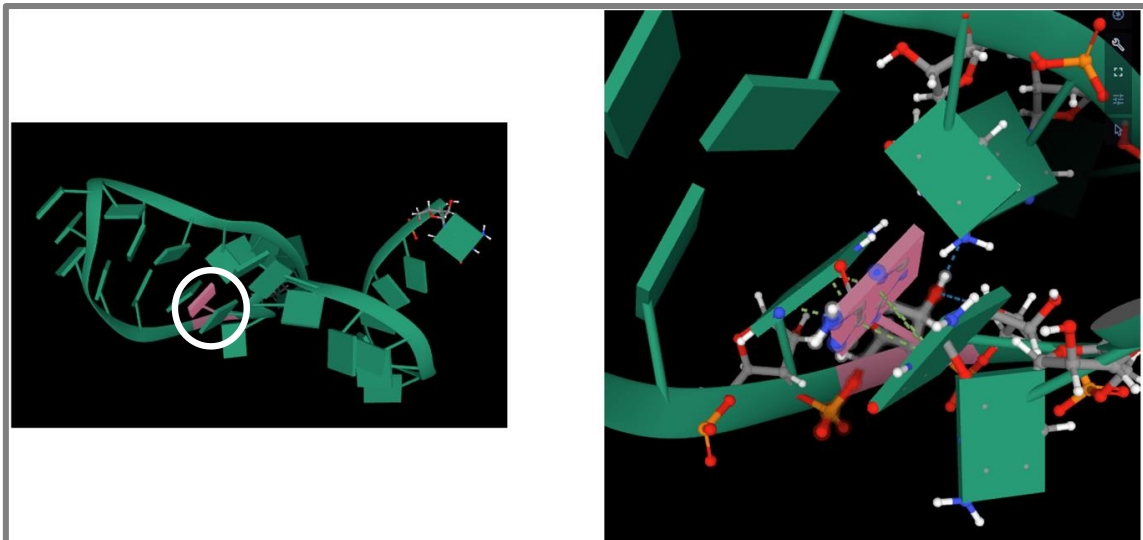
Click on the “Model”, “Opt. Model”, or “Mod. Model” at the right tertiary structure section. PDBe Mol\* Viewer page will open in new window.

“Model” structure was predicted by Rascal. “Opt. Model” and “Mod. Model” structures were relaxed by MD simulations for Rascal model structure within  $\text{Na}^+$  solute respectively. MD simulations from 5 to 10 ns were classified into 10 clusters according to their structural similarities using a k-means method. Ten representative structures for each cluster are stored as the optimized model.

The tertiary structure can be directly confirmed.



Click on the specific nucleotide on this viewer. Some interactions between its nucleotide and other nucleotides can be confirmed.

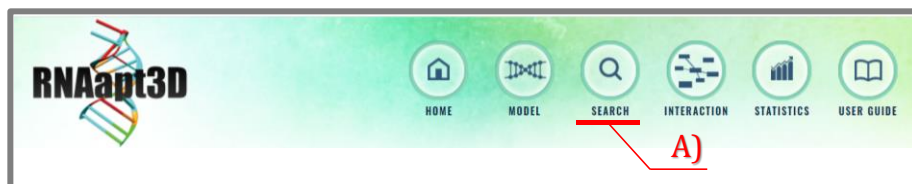




## 2.2 Search for RNA motif

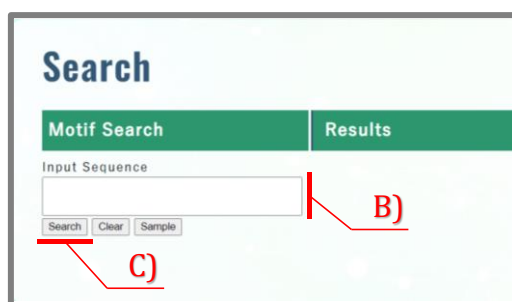
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You can search RNA sequence in RNAapt3D database.



### A) Navigate to search page

Click on the “Search” at the top.



### B) Enter the RNA sequence

Enter the RNA sequence in Motif Search, where the input sequence can be in upper or lower case. If you click “Sample” button, an example sequence will be entered.

### C) Execute Search

Click on the “Search” button, Motif search will take a few tens of seconds.

Some entries containing a given RNA sequence and the predicted base flip positions for these entries will be displayed.

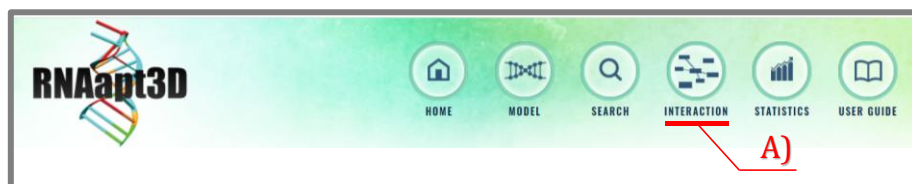
The screenshot shows a web interface for a Motif Search. On the left, under the heading "Search", there is a "Motif Search" section with an "Input Sequence" field containing "UUU" and buttons for "Search", "Clear", and "Sample". On the right, under the heading "Results", it displays "Number of matches: 5" with a download icon. A red arrow points from the word "Download" to this icon. Below this, the results are listed for three motifs: **monad0024** (CGGAAUCAGUGAAUGCUUAUACAUCG), **monad0049** (AAUGAGUGGUUUUUCGUU), and **monad1011** (UUGCUUGGAAUGGUAUAGUCUCUAGGUGUGUA). Each motif is followed by a list of predicted base flip positions, such as (24-1) through (24-5) for monad0024 and (49-1) through (49-4) for monad0049.

Search result can be downloaded by clicking download icon.

### 3 Interaction

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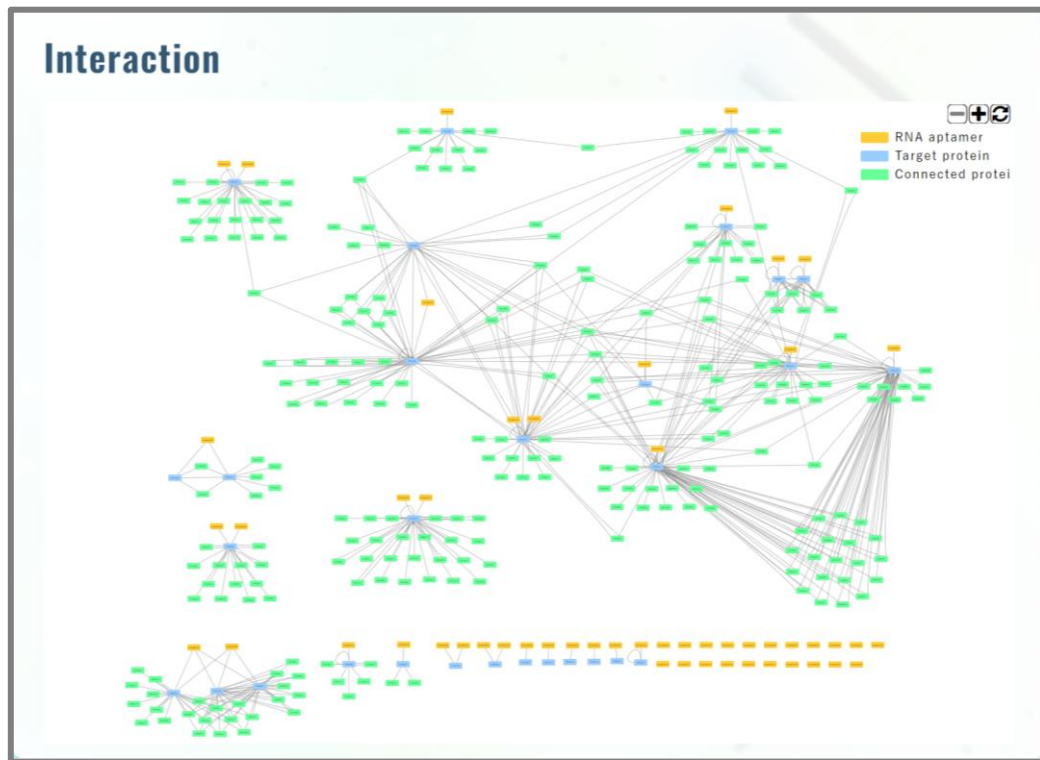
You can check interactions between aptamer and protein, and between protein and protein.



#### **A) Move to interaction page**

Click on the “Interaction” at the top menu.

It shows RNA aptamer (orange square)-Target proteins (blue square) interactions. The proteins (green square) connected to the target proteins (blue square) are obtained by projecting on protein-protein interaction network of Human Protein Reference Database.



The + and- signs in the upper right zoom in and out of the network diagram.

## 4 Statistics

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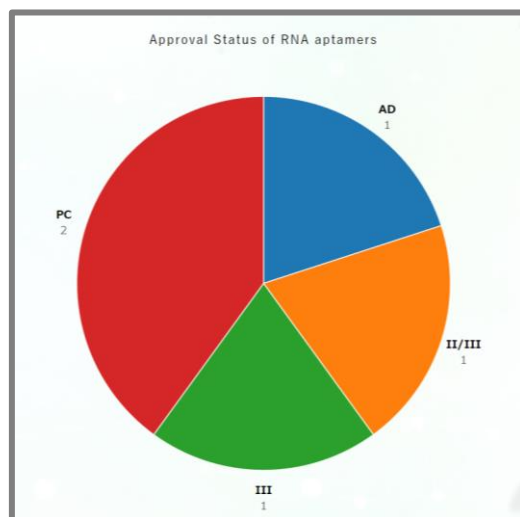
Statistical information is on Statistics page.



### A) Move to statistics page

Click on the “Statistics” at the top.

The number of RNA aptamer included this database for each clinical phase can be confirmed.



Following shows legend for this chart.

**Clinical Trial Phase**

AD	Approved Drug
II/III	Phase II/III
III	Phase III
PC	Pre-Clinical Phase

## 5 Contact Us

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**RNAapt3D**

URL: <https://rnaapt3d.medals.jp>



If you have any questions or comments, please contact the following e-mail address.

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