

The Bioinformatic Analysis of  
Function Differentiation on  
Human Aurora A and Aurora B  
(AURORA A与AURORA B功能分化的生物信息学分析)

Group08

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Members : 林巧玉、

Reporter : 赵梓伊

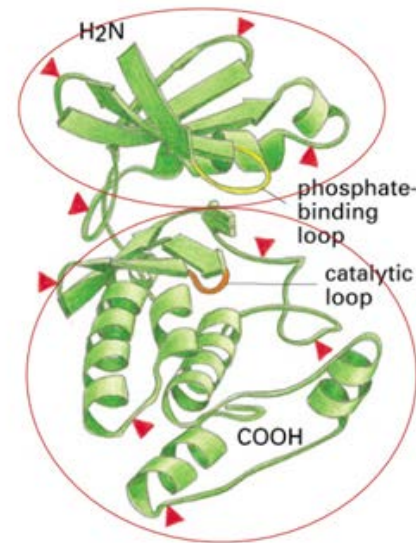
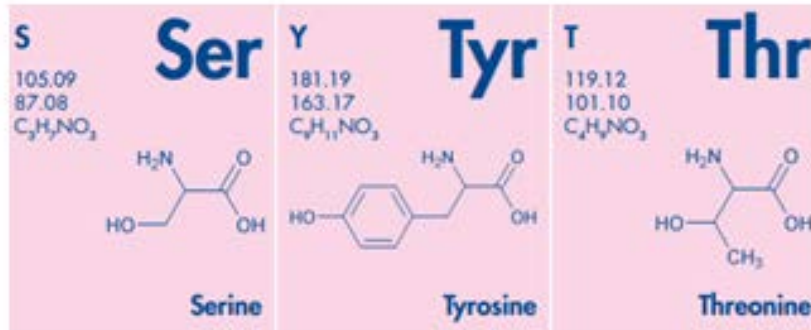
2014/06/19

# Outline

- **Background**
- **Research purpose**
- **Results & Discussion**
- **Acknowledgement**

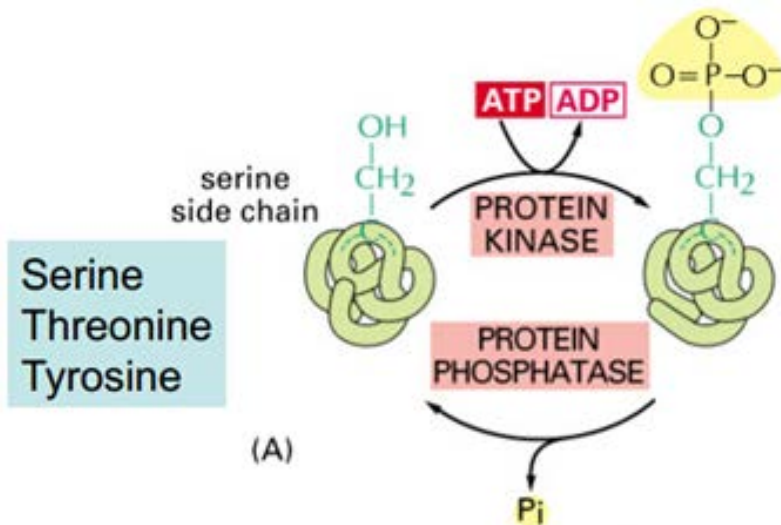


# Protein Kinase



3-D structure of a typical protein kinase domain

- N: ATP-binding
- C: catalytic loop



(Wang Yingzhen.)



# History of Aurora

## Isolation and Characterization of Chromosome-Gain and Increase-in-Ploidy Mutants in Yeast

Clarence S. M. Chan<sup>1</sup> and David Botstein<sup>2</sup>

*Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139*

Manuscript received November 5, 1992

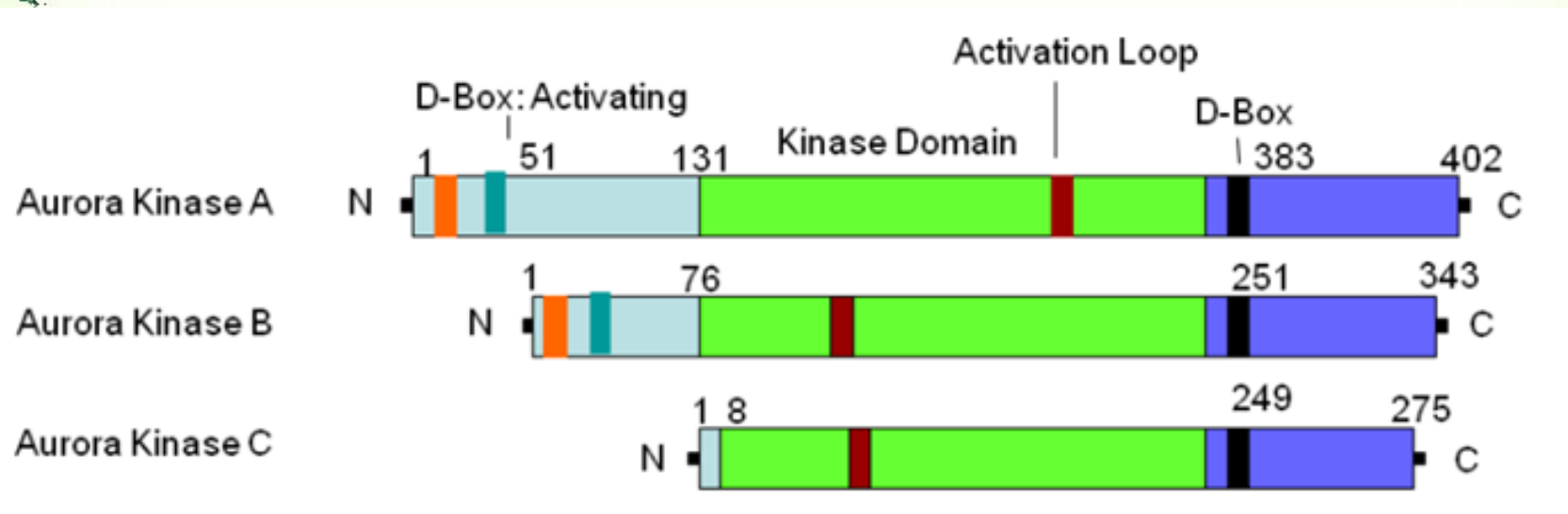
Accepted for publication July 15, 1993



([www.Baidu.com](http://www.Baidu.com))



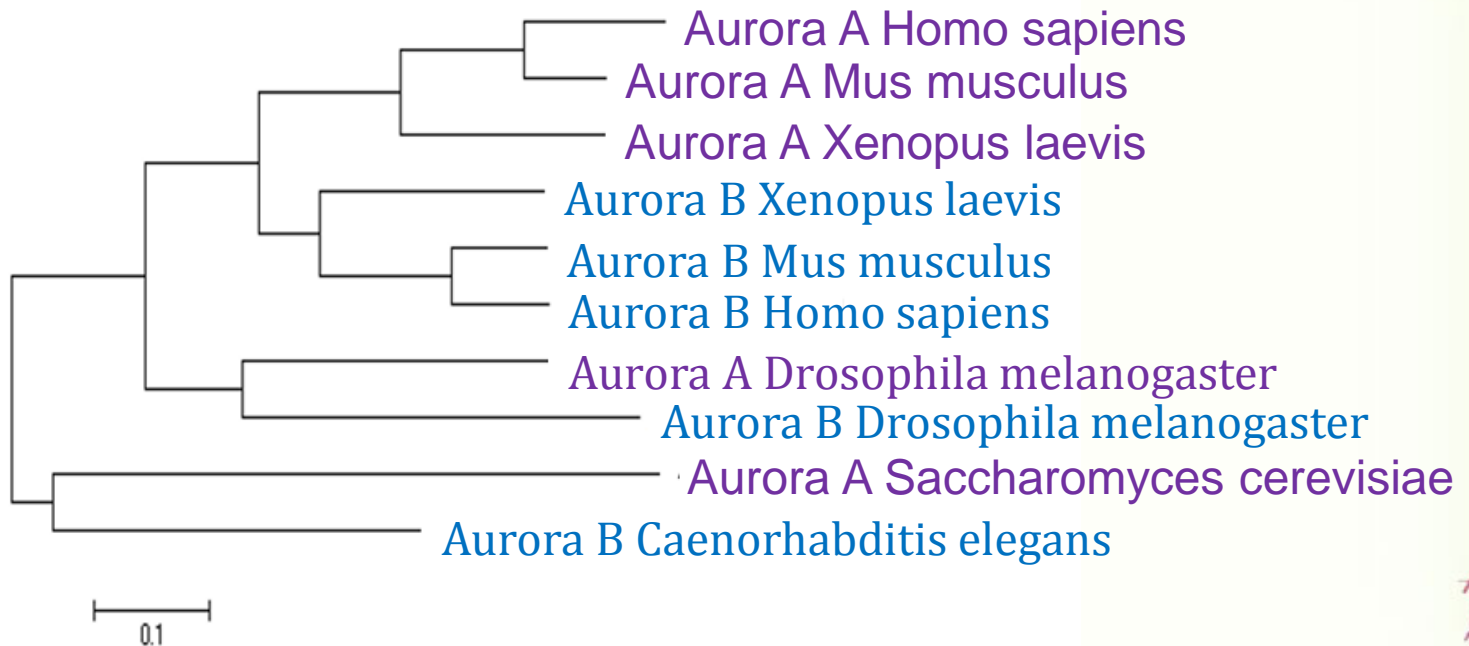
# Aurora Kinase Family



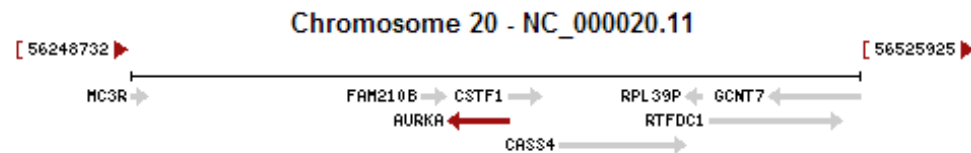
( Dar et al. Mol Cancer Ther. 2010 )



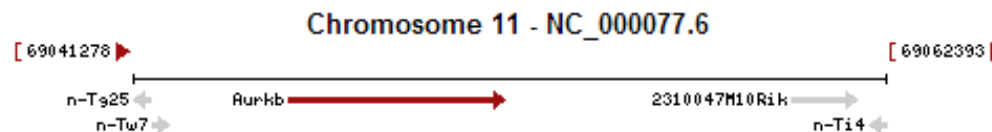
# BLAST&Tree



Aurora A



Aurora B



# Sequence alignment

## CDS Alignment

### Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
1308	1955.0	713/1308 (54.5%)	713/1308 (54.5%)	369/1308 (28.2%)

### Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
1262	1960.0	711/1262 (56.3%)	711/1262 (56.3%)	326/1262 (25.8%)

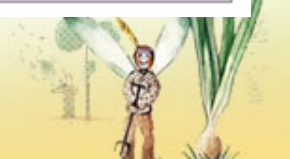
## AA Alignment

### Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
426	1055.0	212/426 (49.8%)	251/426 (58.9%)	105/426 (24.6%)

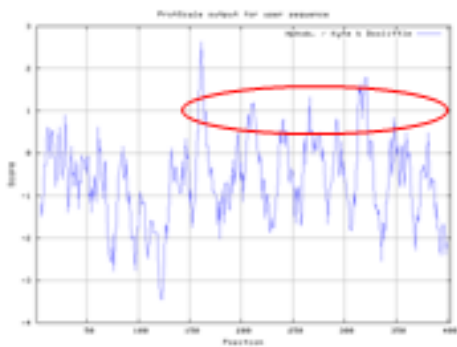
### Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
343	1059.0	212/343 (61.8%)	251/343 (73.2%)	26/343 (7.6%)

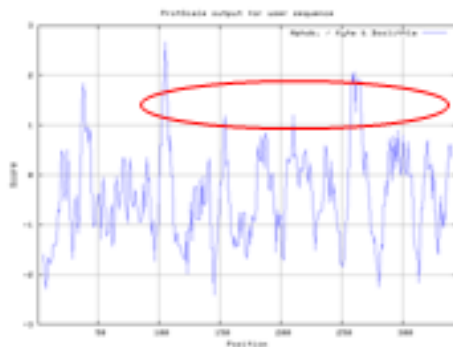


# Characteristics

## Hphob./ Kyte & Doolittle

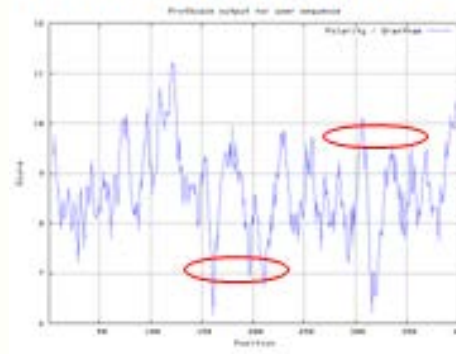


Aurora A

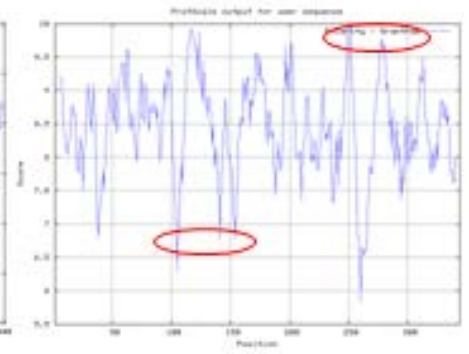


Aurora B

## Polarity/Grantham

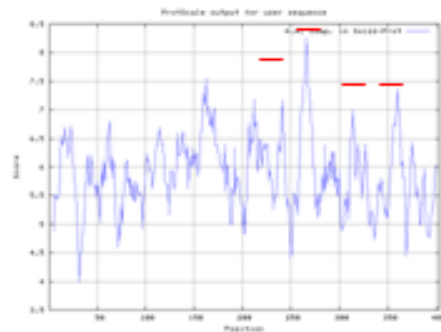


Aurora A

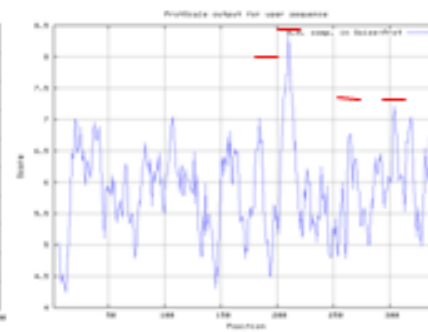


Aurora B

## AA composition in SWISS-prot



Aurora A



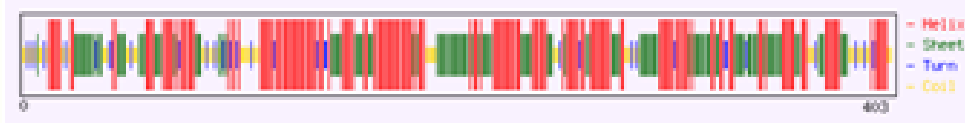
Aurora B





# Secondary Structure

## Aurora A



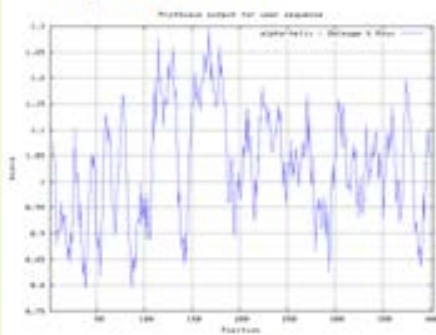
Percent: H: 68.5 E: 54.6 T: 13.6

## Aurora B

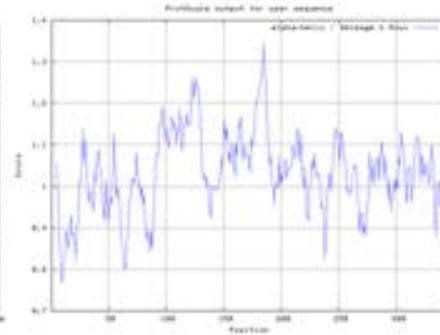


Percent: H: 66.6 E: 56.4 T: 16.9

## Alpha-helix

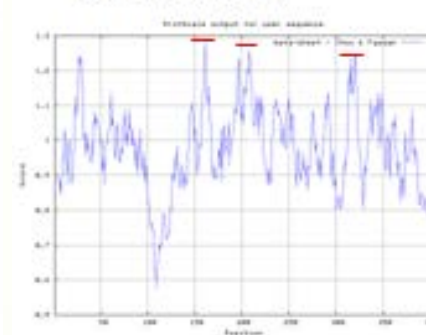


Aurora A

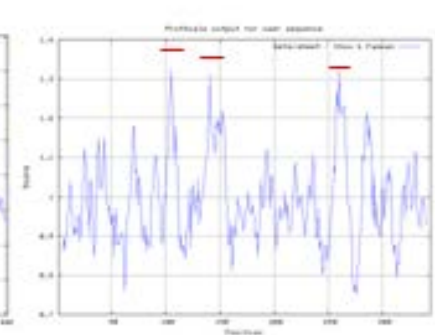


Aurora B

## Beta-sheet



Aurora A

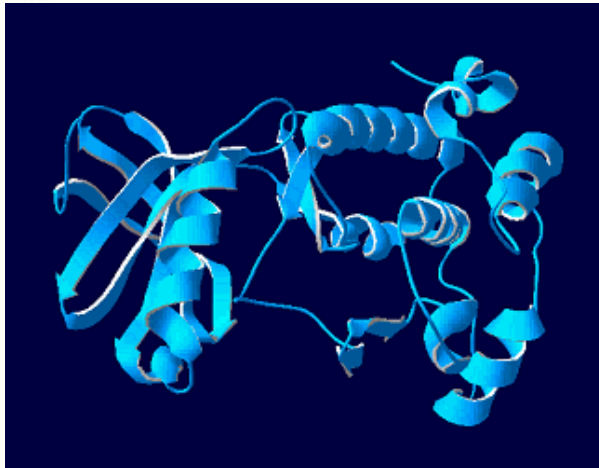


Aurora B

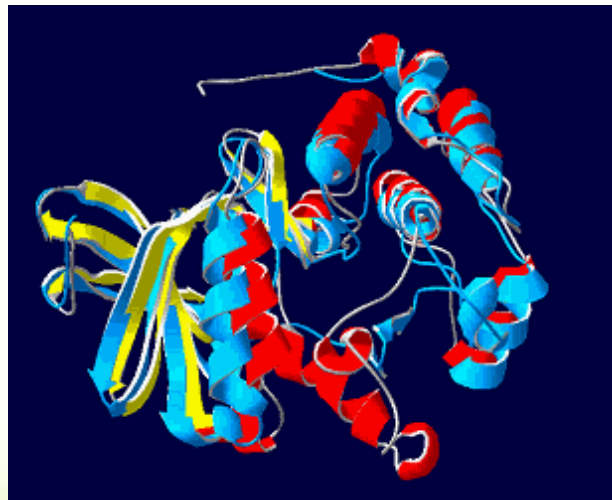
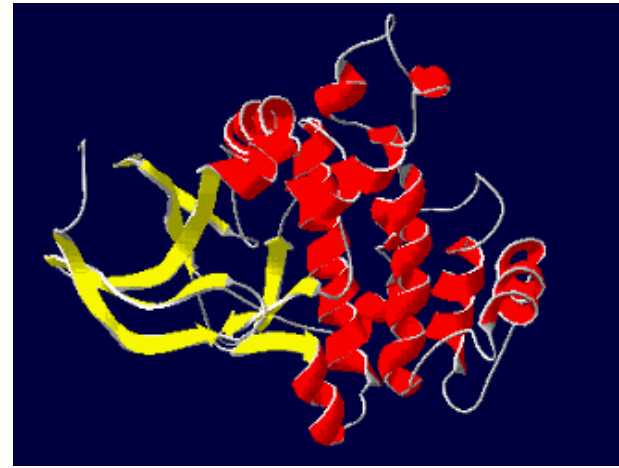


# SWISS-MODEL

hAurora A



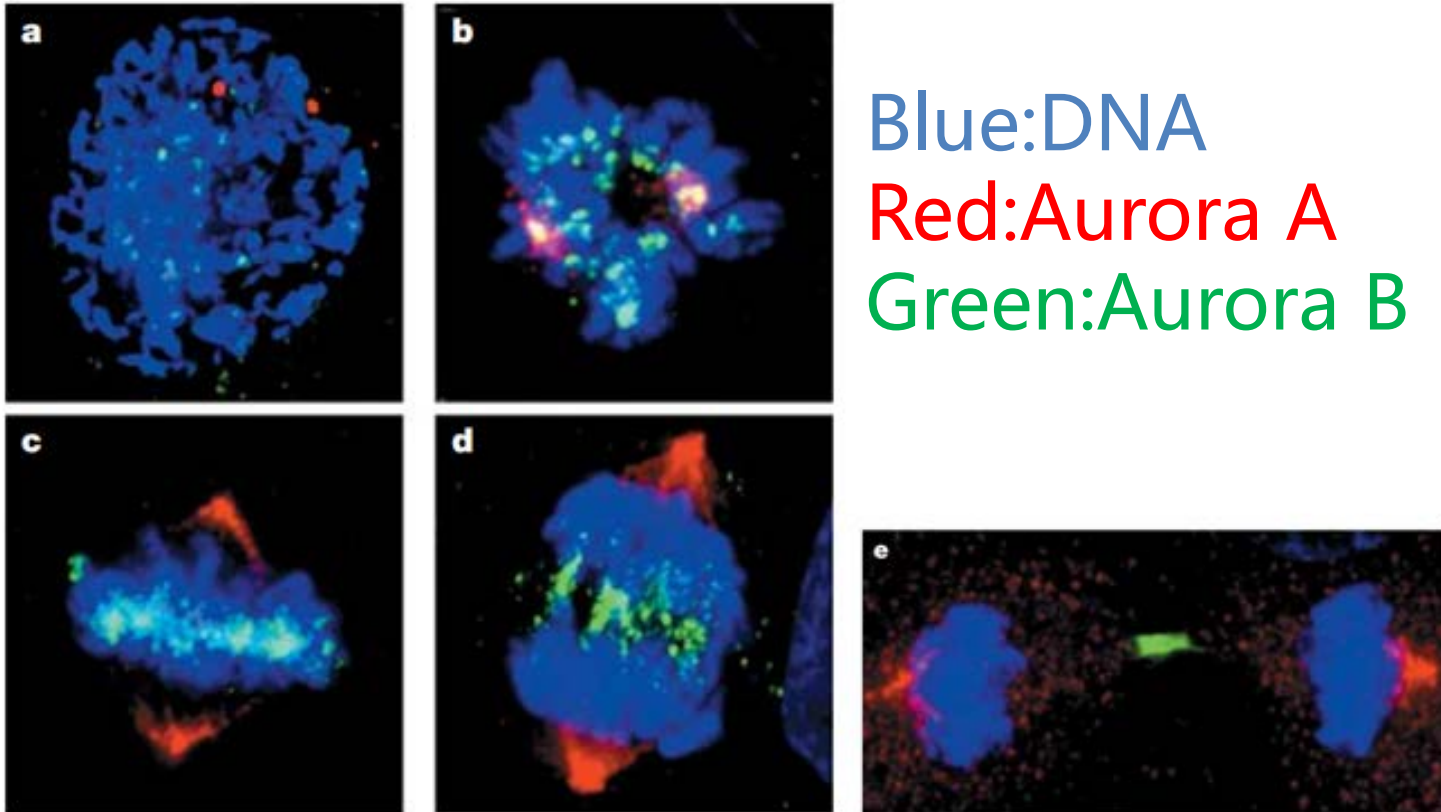
hAurora B



Magic Fit(CA)



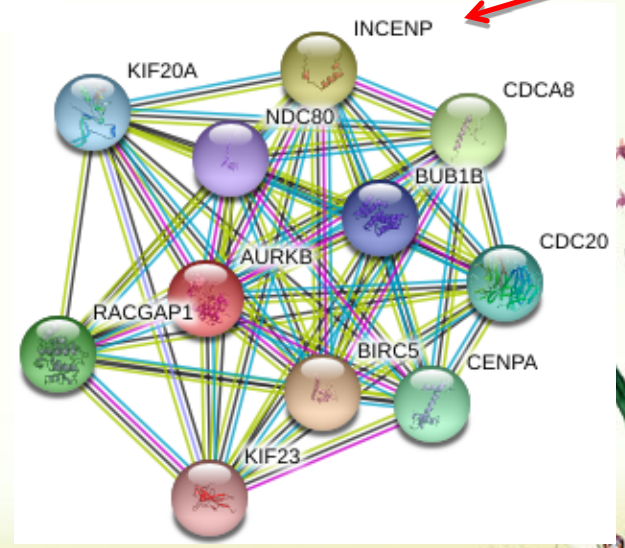
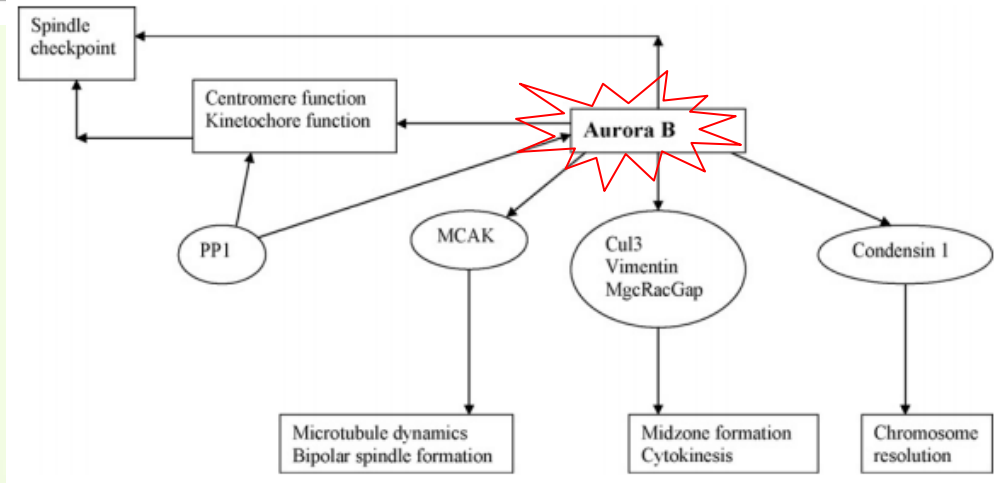
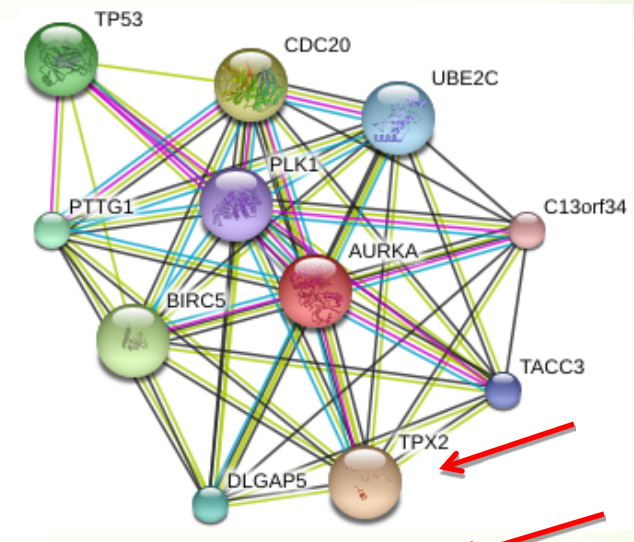
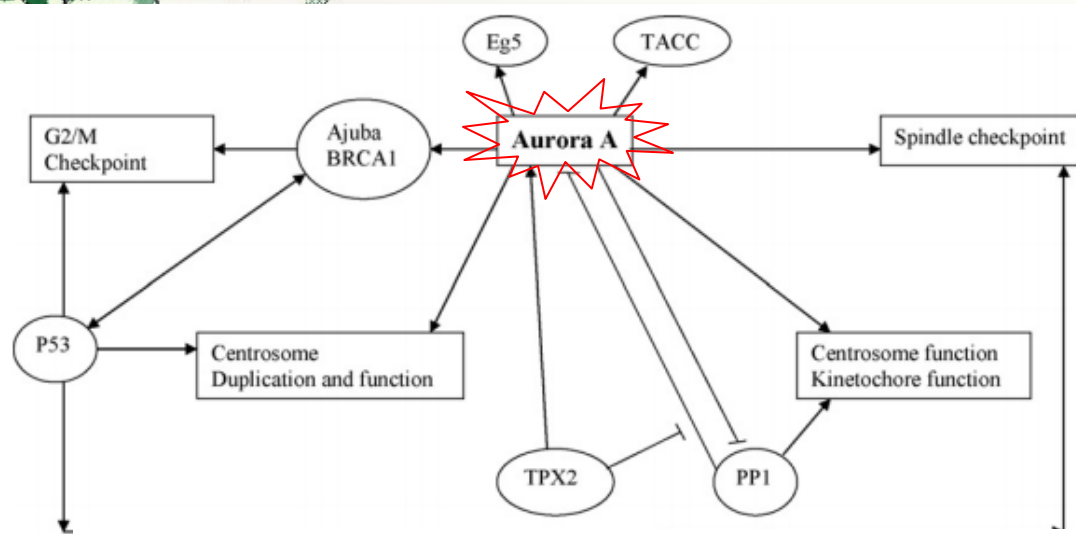
# Localization



(Nicholas Keen ,Stephen Taylor. Nature Reviews Cancer. 2004)

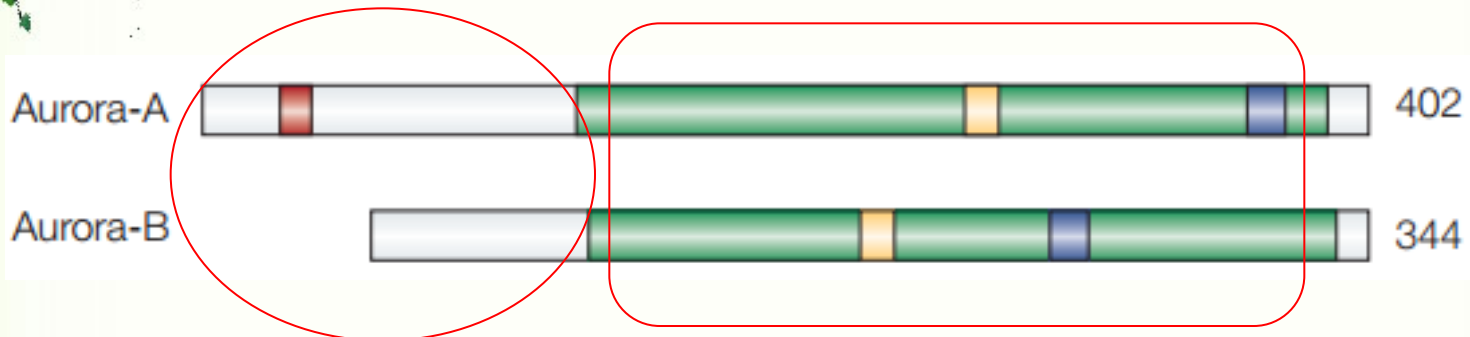


# Function of Aurora A & Aurora B



( J.J.E.M. Kitzen et al. Critical Reviews in Oncology/Hematology .(2010) )

# What drives the differences?



N-terminal?

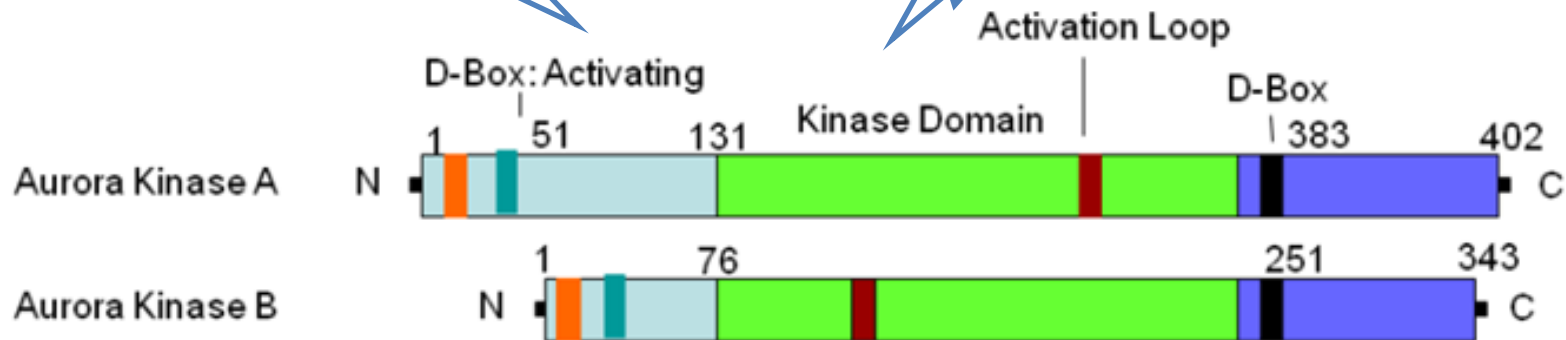
Catalytical domain?



# Fragment truncation

N-terminal  
Aurora A 1-132 aa  
Aurora B 1-76 aa

Kinase domain  
Aurora A 133-383aa  
Aurora B 77-327 aa



( Dar et al.Mol Cancer Ther. 2010 )

# N-terminal

Needle

Pairwise Alignment Result

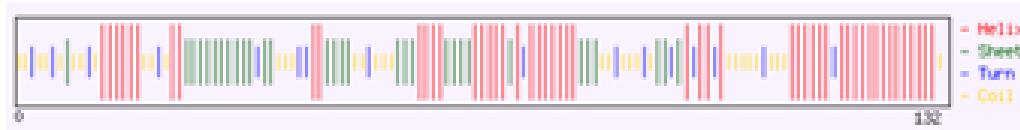
LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
152	27.0	19/152 (12.5%)	28/152 (18.4%)	96/152 (63.2%)

Water

Pairwise Alignment Result

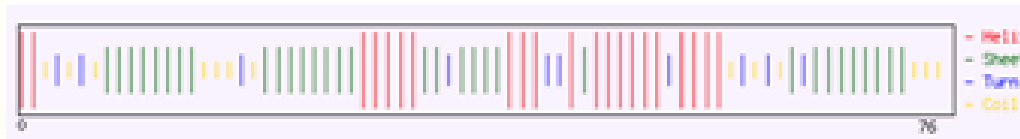
LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
84	35.5	22/84 (26.2%)	32/84 (38.1%)	30/84 (35.7%)

## Aurora A



Percent: H: 56.8 E: 38.6 T: 16.7

## Aurora B



Percent: H: 43.4 E: 52.6 T: 23.7



# Pertinent Literature

[Cell Cycle 4:6, 784-789; June 2005]; ©2005 Landes Bioscience

Report

## The Aurora A and Aurora B Protein Kinases

A Single Amino Acid Difference Controls Intrinsic Activity and Activation by TPX2

Molecular Biology of the Cell  
Vol. 20, 3491–3502, August 1, 2009

### **Molecular Distinctions between Aurora A and B: A Single Residue Change Transforms Aurora A into Correctly Localized and Functional Aurora B**

**Fabienne Hans,<sup>\*†</sup> Dimitrios A. Skoufias,<sup>†‡</sup> Stefan Dimitrov,<sup>\*</sup> and Robert L. Margolis<sup>‡§</sup>**

A single amino acid change converts Aurora-A into Aurora-B-like kinase in terms of partner specificity and cellular function

Jingyan Fu<sup>a</sup>, Minglei Bian<sup>a</sup>, Junjun Liu<sup>b</sup>, Qing Jiang<sup>a</sup> and Chuanmao Zhang<sup>a,1</sup>

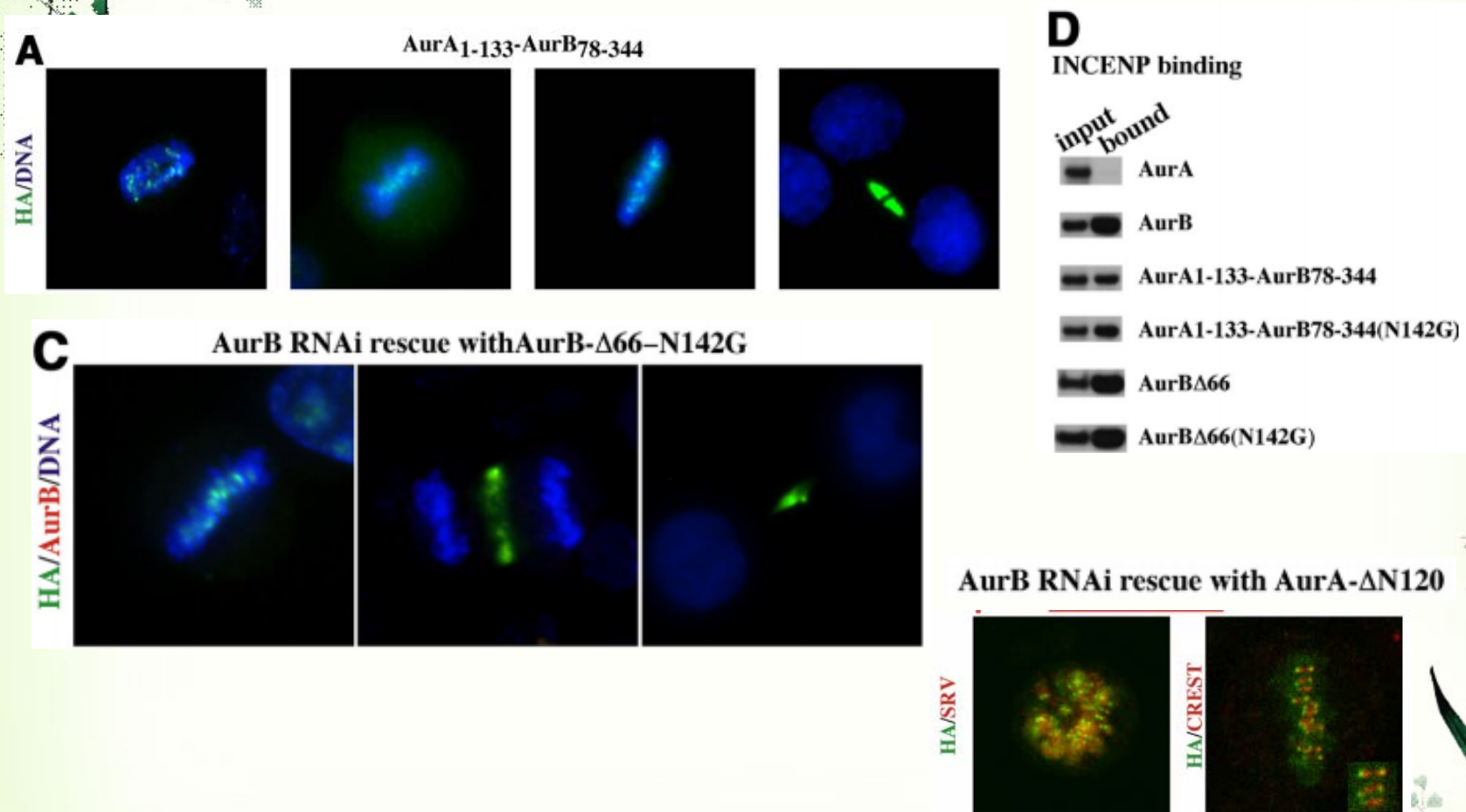
[Author Affiliations](#) ↗

Edited by Don W. Cleveland, University of California at San Diego, La Jolla, CA, and approved March 5, 2009 (received for review January 25, 2009)





# Pertinent Literature



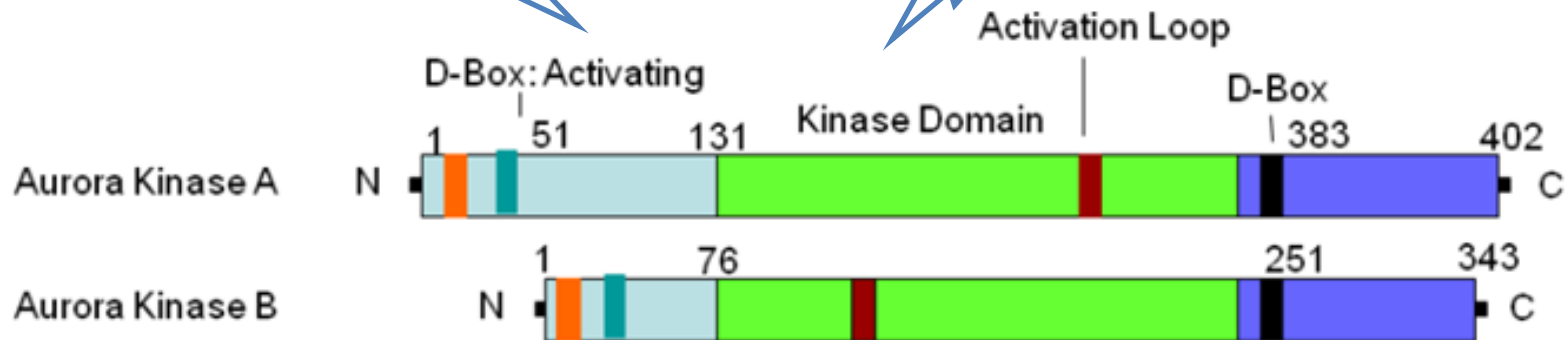
(Fabienne Hans et al., Mol Biol Cell. 2009 Aug;20(15):3491-502)



# Fragment truncation

N-terminal  
Aurora A 1-132 aa  
Aurora B 1-76 aa

Kinase domain  
Aurora A 133-383aa  
Aurora B 77-327 aa



( Dar et al. Mol Cancer Ther. 2010 )

# C-ter Kinase domain



Needle

Pairwise Alignment Result

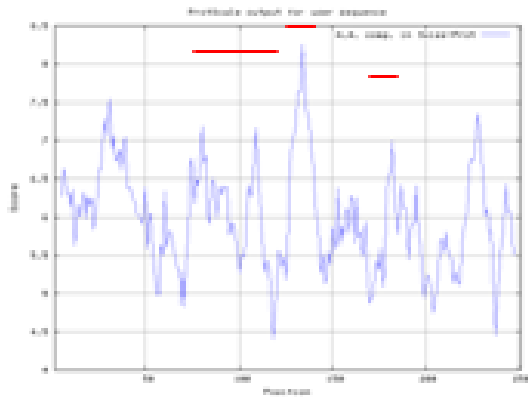
LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
251	1014.0	187/251 (74.5%)	215/251 (85.7%)	0/251 ( 0.0%)

Water

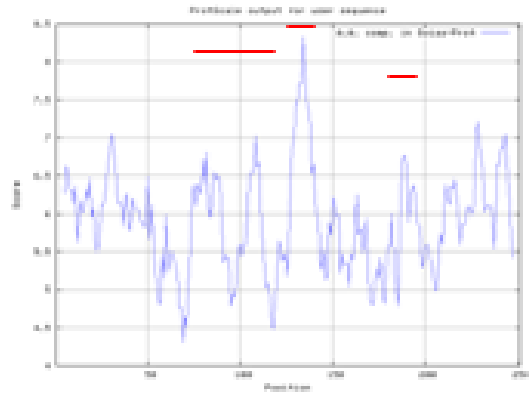
Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
251	1014.0	187/251 (74.5%)	215/251 (85.7%)	0/251 ( 0.0%)

## AA composition in Swiss-Prot



Aurora A

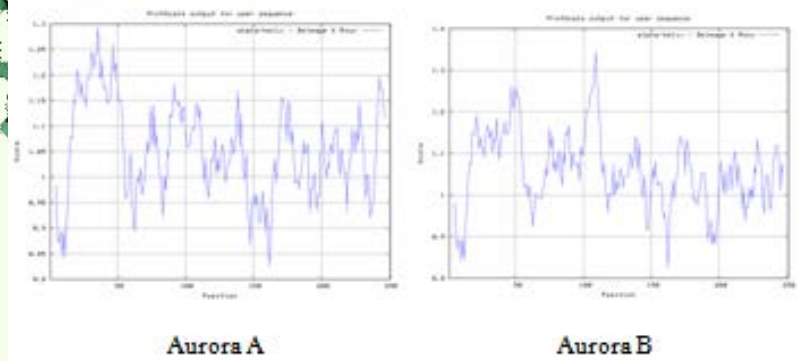


Aurora B

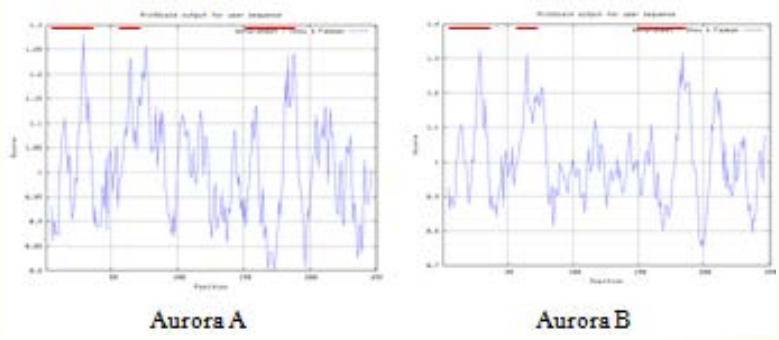


# C-ter Kinase domain

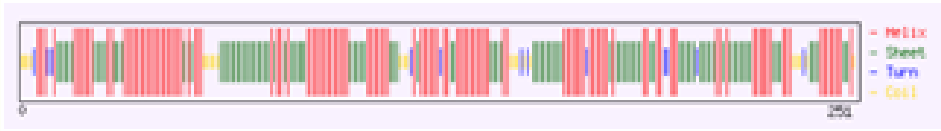
## alpha-helix



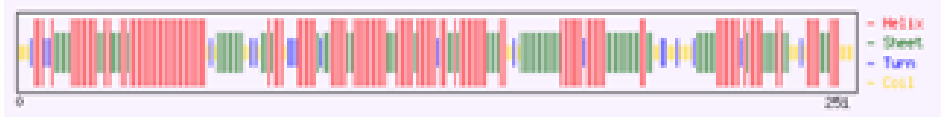
## Beta-sheet



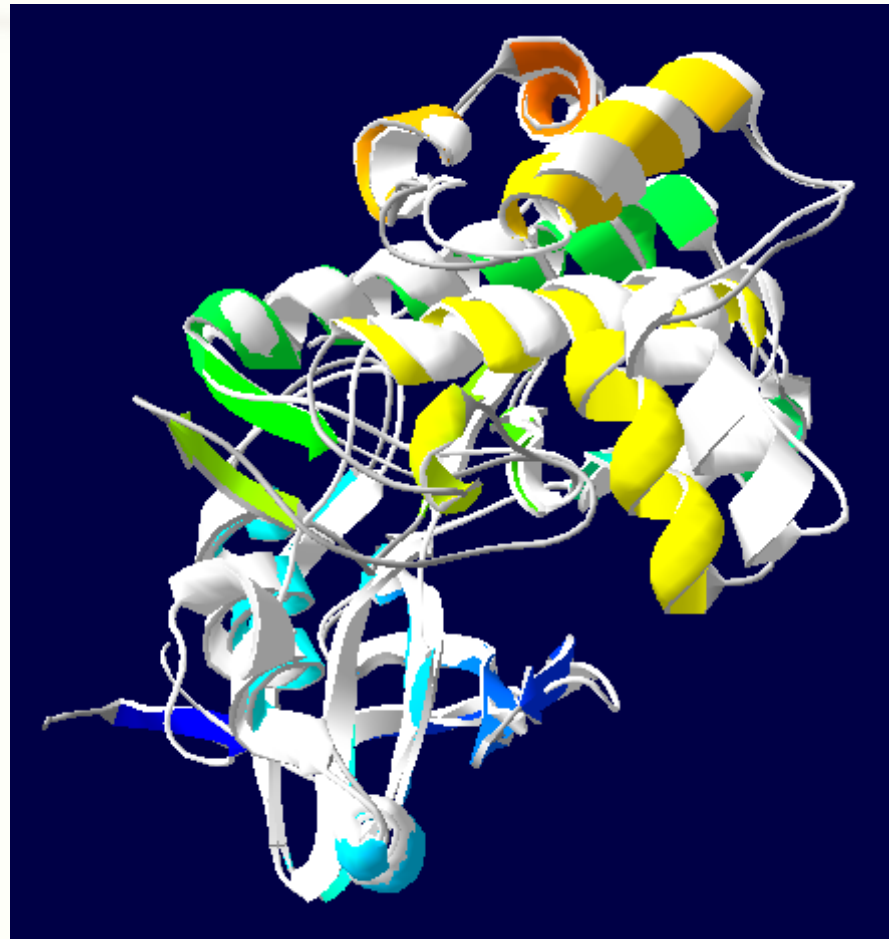
## Aurora A kinase domain ( 133-383aa )



## Aurora B kinase domain ( 77-327aa )



# Magic Fit



**Colorful:**hAurora A (1OL5:122-403)

**White:**hAurora B (4AF3:70-338)



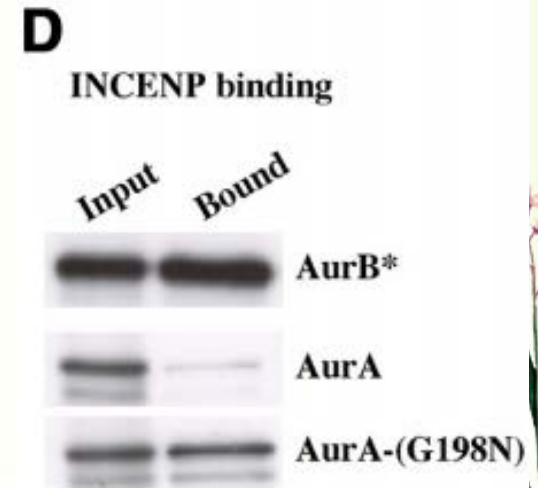
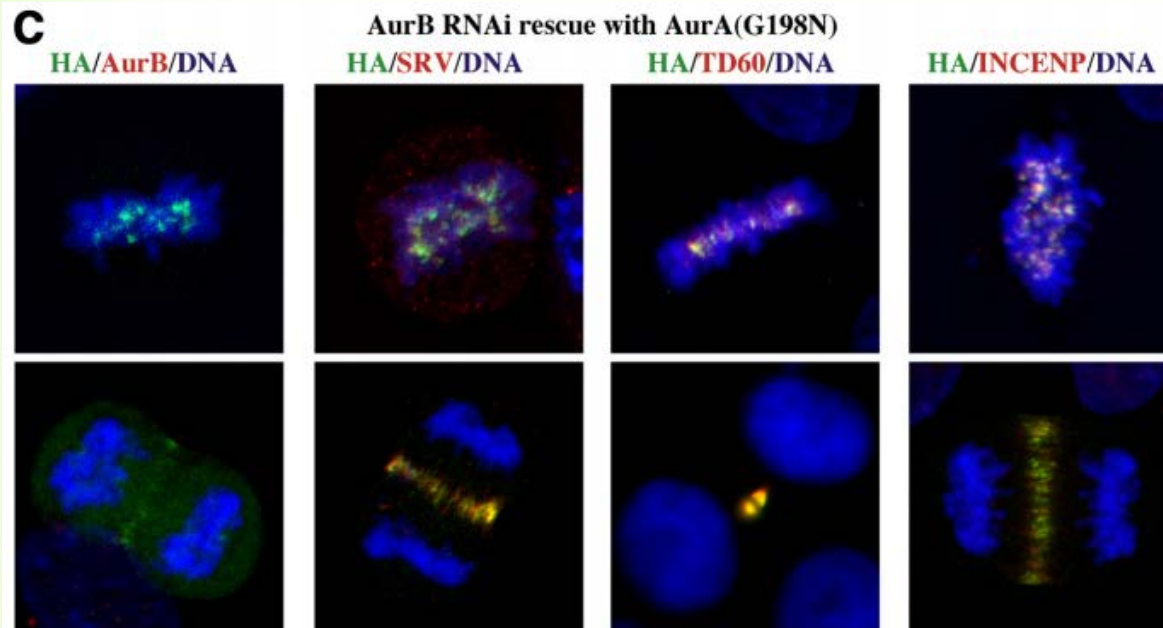


# AurA G198 & AurB N142

142

hAurB REIEIQ~~AHLHHPN~~ILRLY~~NYFYD~~RRRIYLLILEYAPR  
 hAurA REVEIQSHLRHPN~~ILRLYGYF~~HDATRVYLLILEYAPL

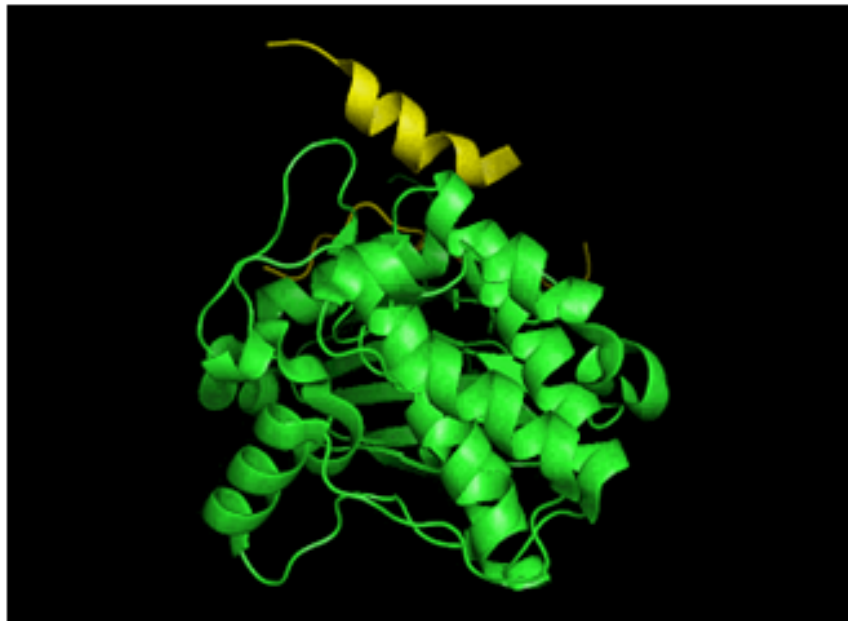
198



(Fabienne Hans et al., Mol Biol Cell. 2009 Aug;20(15):3491-502)

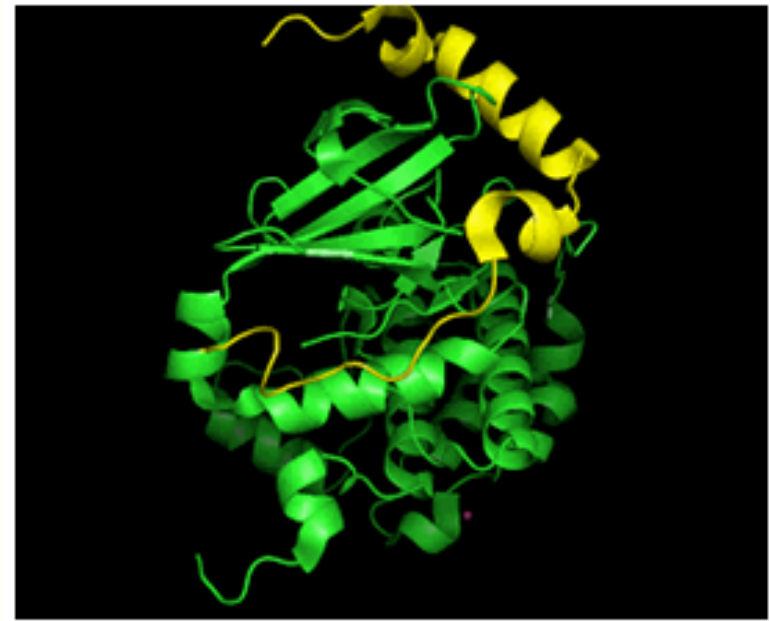
# Interaction

Aurora A with TPX2

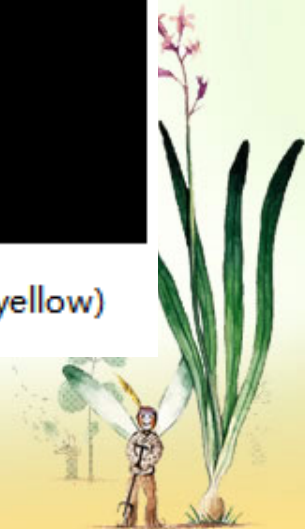


hAurora A(green); TPX2(yellow)  
PDB ID:1OL5

Aurora B with INCENP

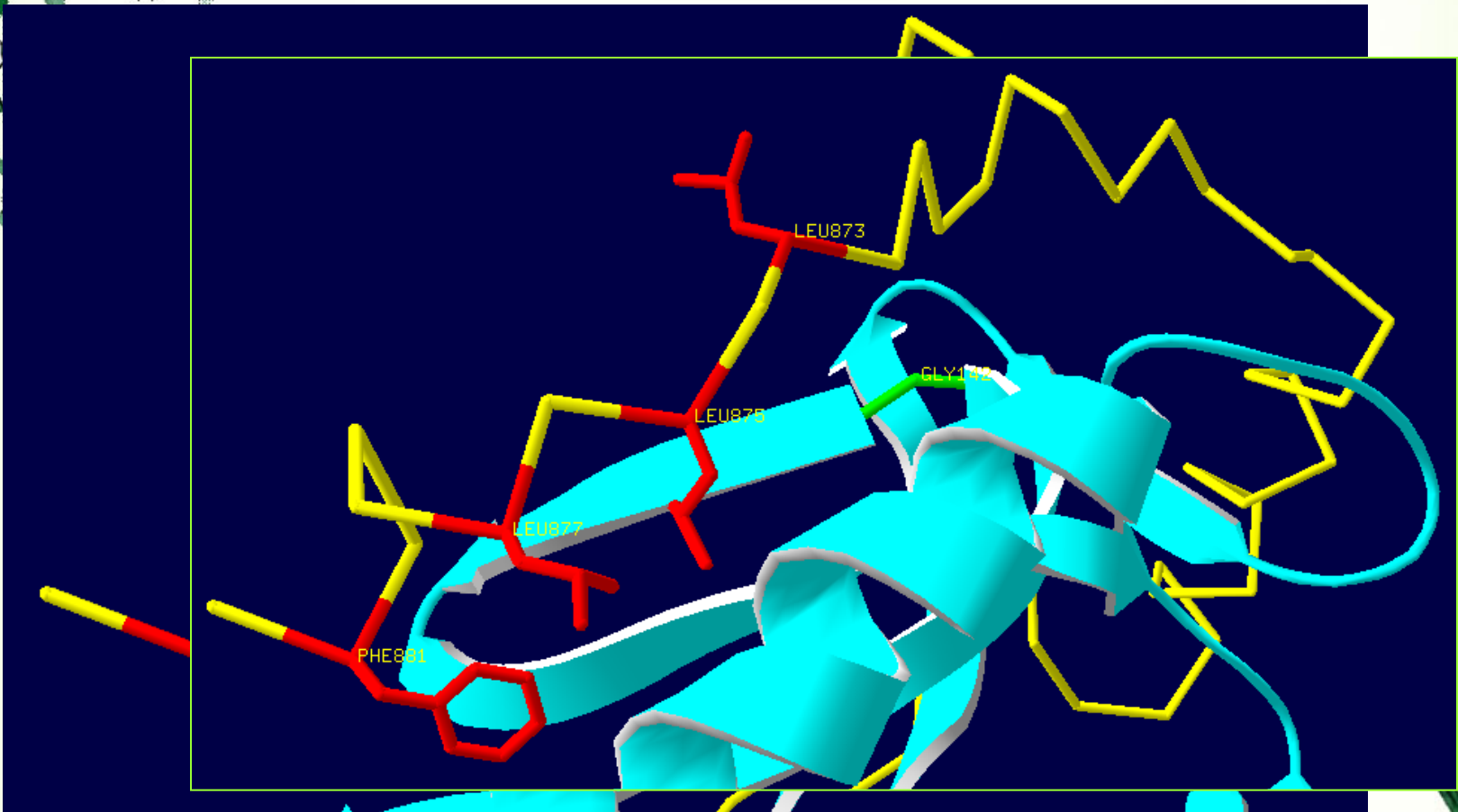


hAurora B(green); INCENP(yellow)  
PDB ID:4AF3





# Aurora-B<sup>N142G</sup>

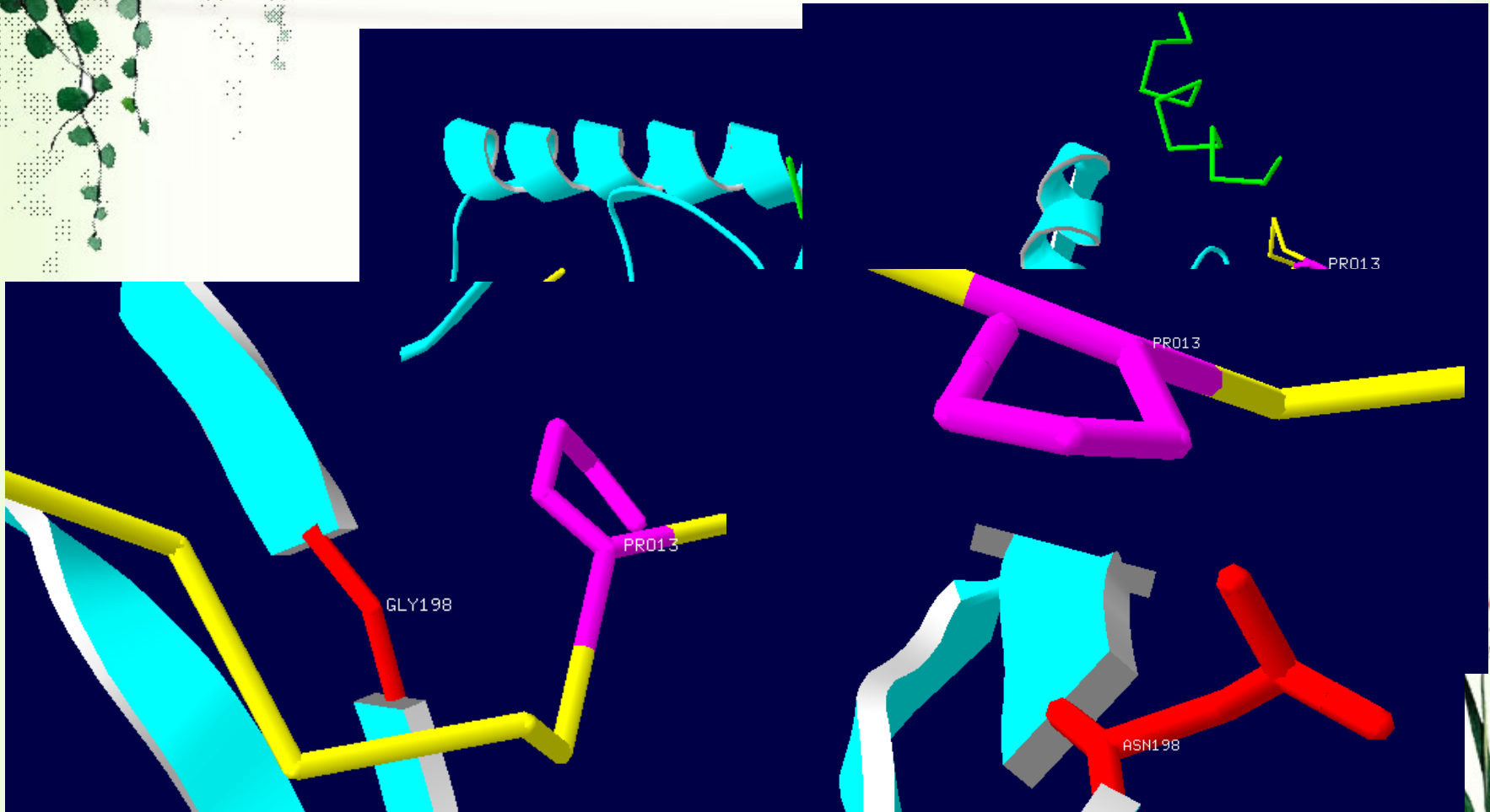


hAurora B ( blue )

INCENP<sup>840-882</sup> ( yellow )



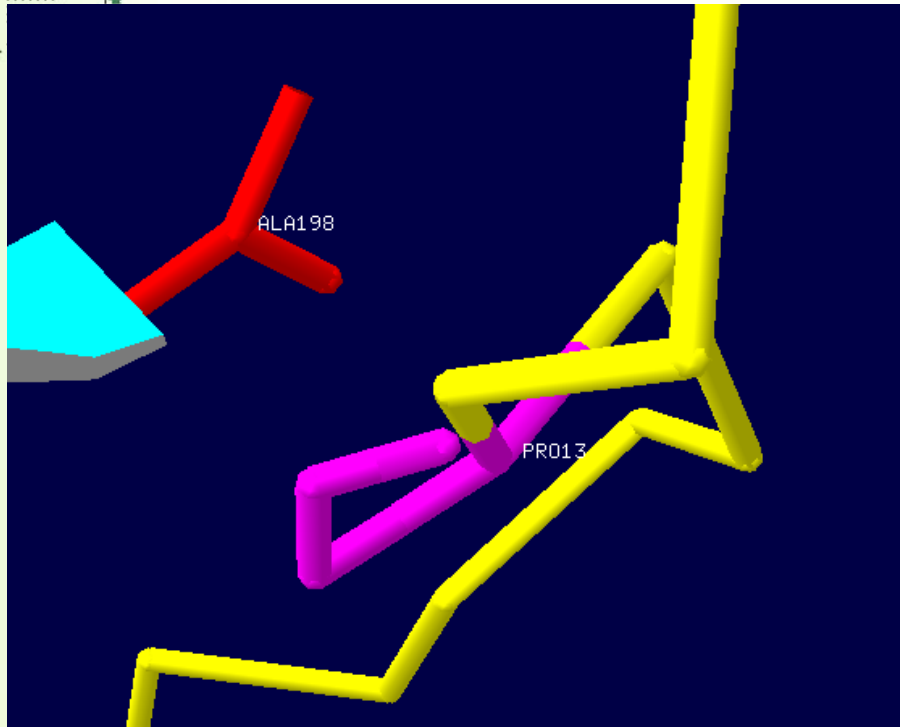
# Aurora A<sup>G198N</sup>



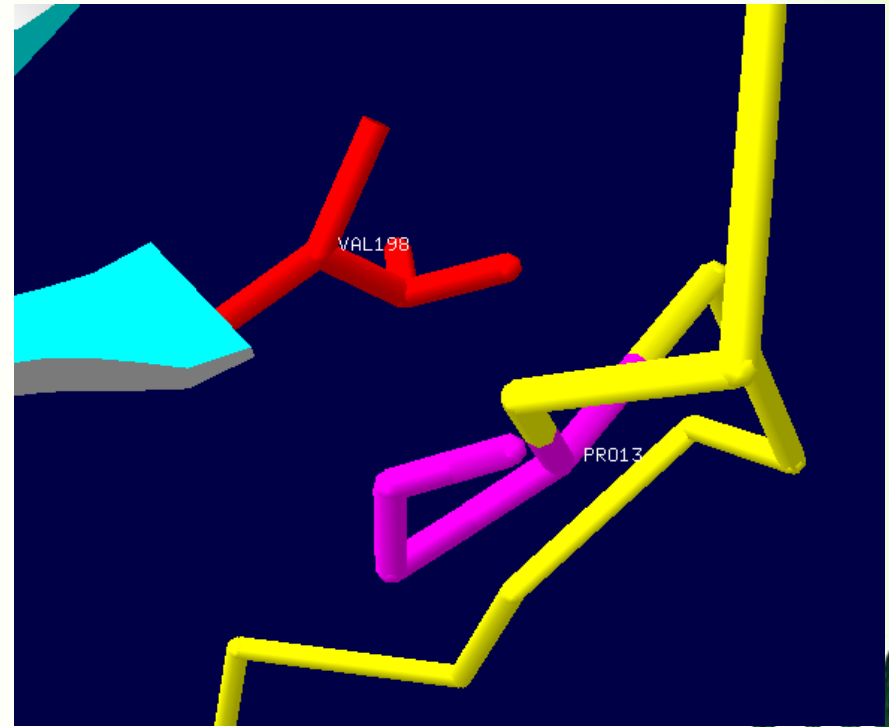
hAurora  
TPX2<sup>27-21</sup> ( yellow )  
TPX30-43 ( green )



# Aurora A<sup>G198A</sup>

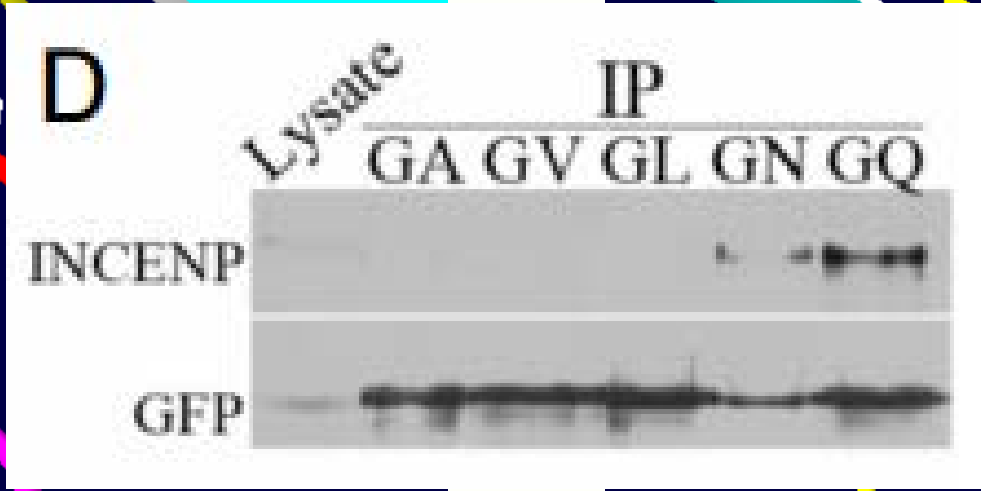


# Aurora A<sup>G198V</sup>



Aurora A<sup>G198L</sup>

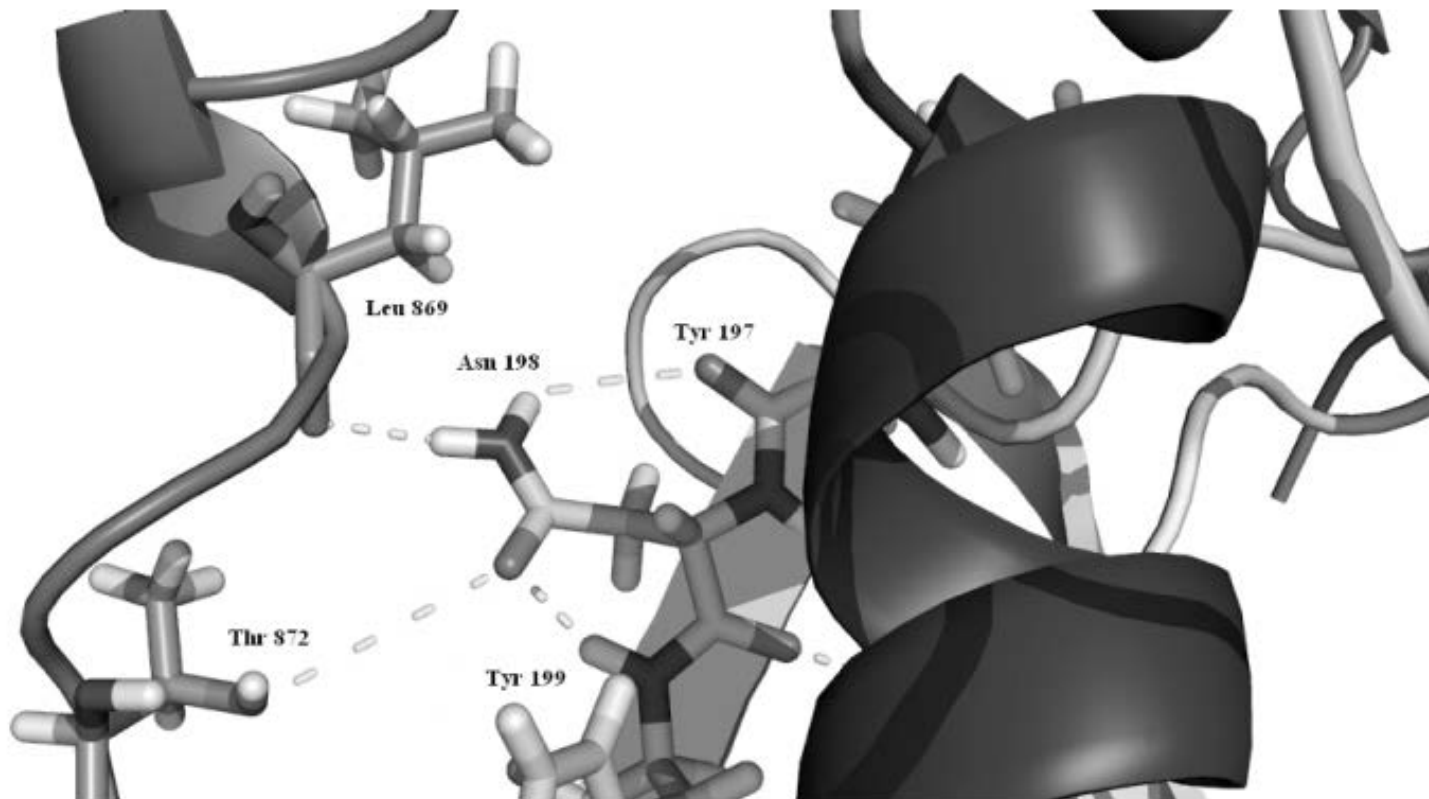
Aurora A<sup>G198Q</sup>



# Aurora A<sup>G198N</sup> - INCENP complex

Structural Basis for Binding of Aurora-A<sup>G198N</sup> - INCENP Complex

Protein & Peptide Letters, 2013, Vol. 20, No. 11 1253



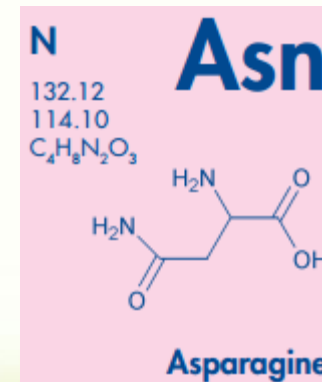
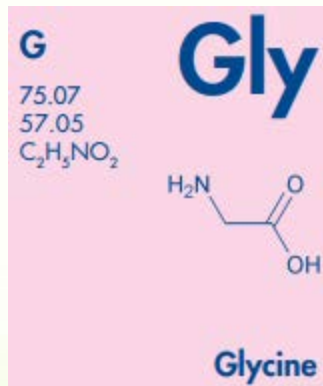
(Karunakar Tanneeru and Lalitha Guruprasad. Protein & Peptide Letters 2013.)

# Conclusion

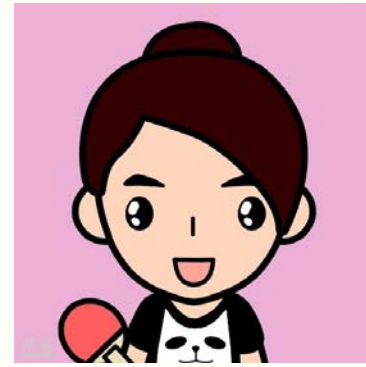
Butterfly effect-like :

NOT N-terminal !

But a single amino acid change in C-ter Kinase domain makes big difference!



# Acknowledgement



**Thank you!**