



Department of Chemistry
UNIVERSITY OF CALIFORNIA, IRVINE

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RNA Interference-Mediated Choline Kinase Suppression in Breast Cancer Cells Induces Differentiation and Reduces Proliferation

- RNAi knockout of choline kinase for the first time in the breast cells.

Cell?

What is cancer?

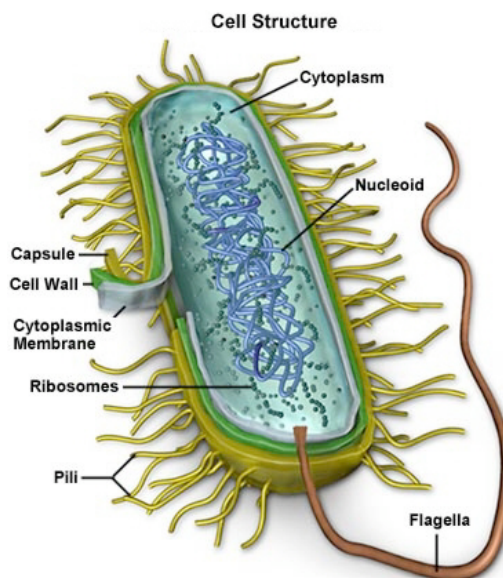
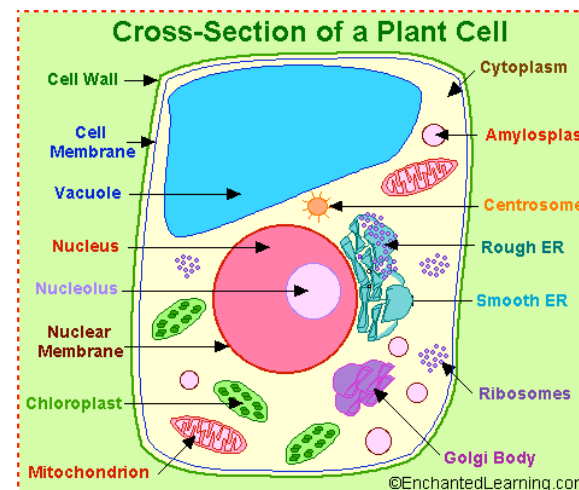
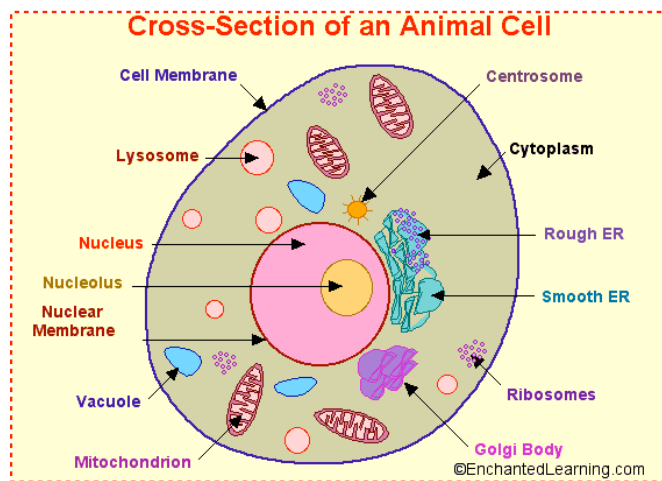
What is RNA interference & choline kinase?

What they did?

Our work.



Cell : The basic unit of any living organism that carries on the biochemical processes of life.



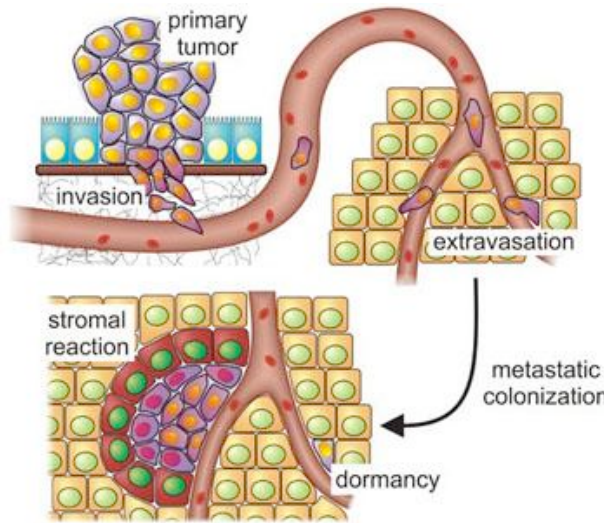
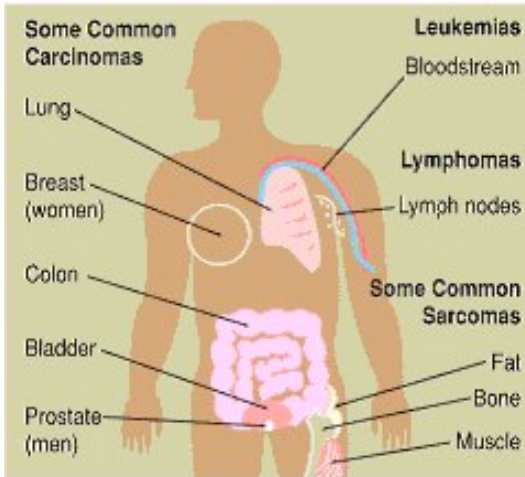
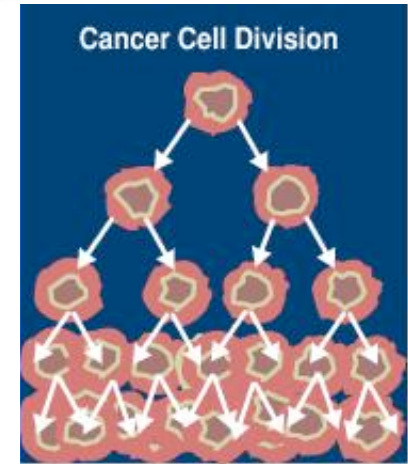
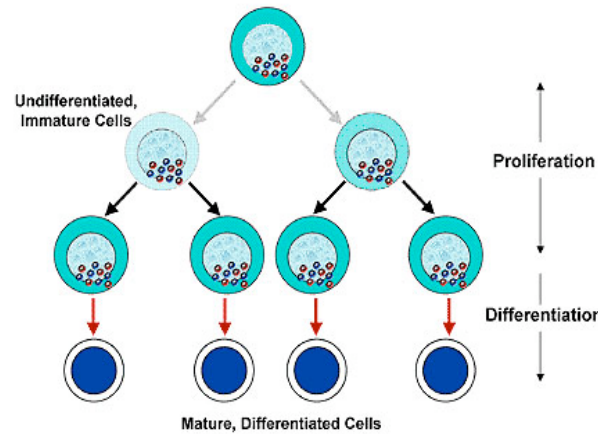


What is Cancer?

Cell division is highly controlled – few cells in human body undergo mitosis (cell division)

Cancer involves uncontrolled cell growth

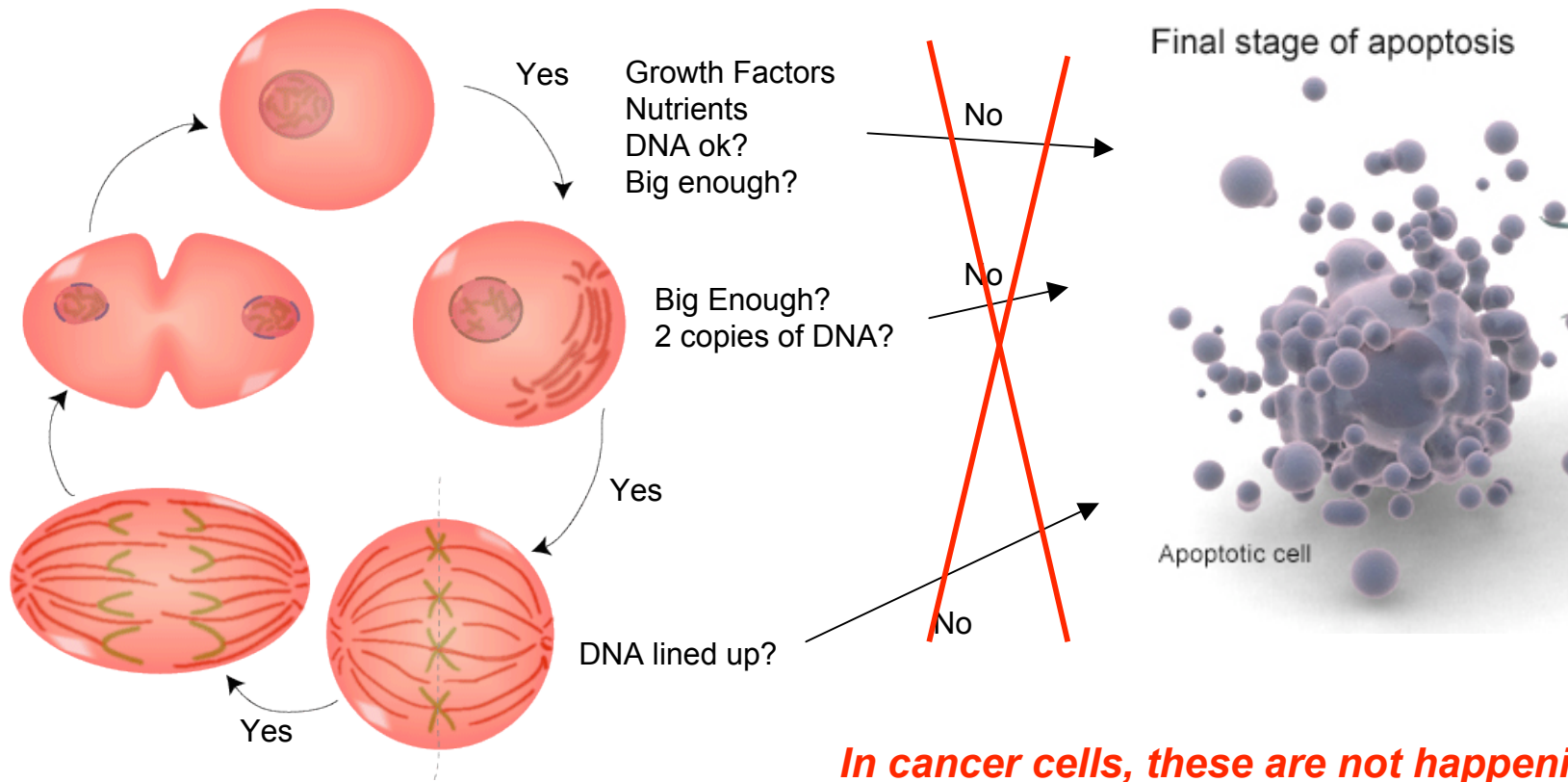
Cancers are more likely to arise from tissue that can proliferate



Cancers can invade surrounding tissue. A cancer that enters the blood/lympatic system can spread out (Metastasis)



Dividing cells pass through 3 checkpoints : Dividing cells are very sensitive to even small DNA damage or changes



In cancer cells, these are not happening



Why cancer happens?

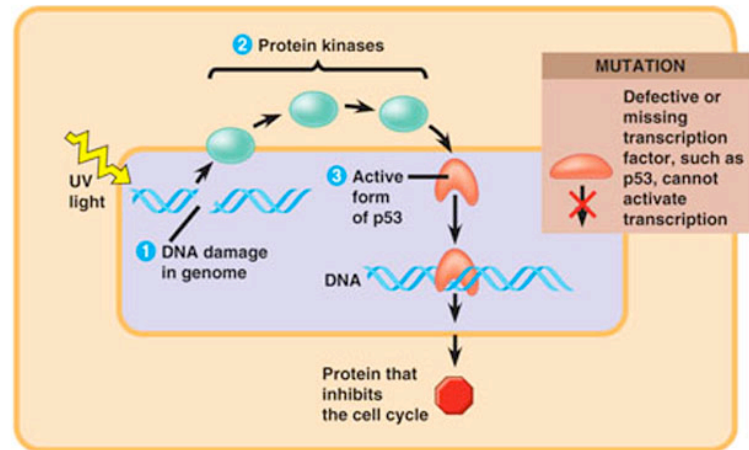
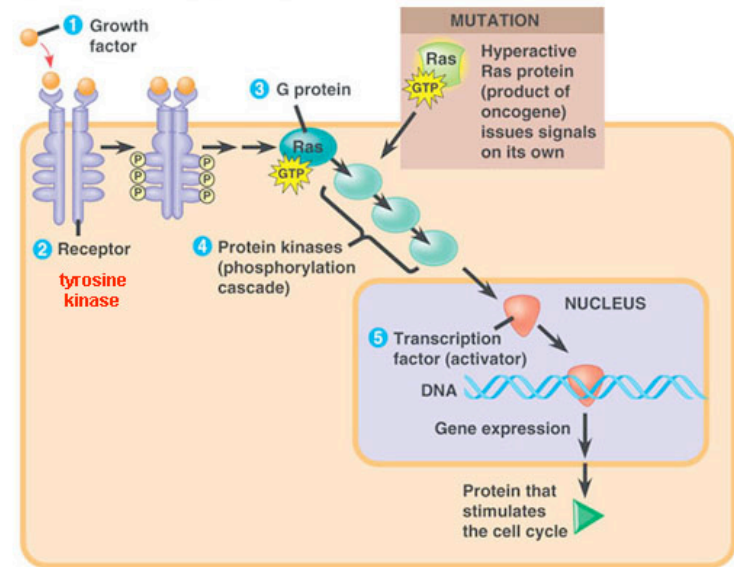
Cell growth is controlled by three stages

The acceleration: growth factors

The transmission: kinase cascades

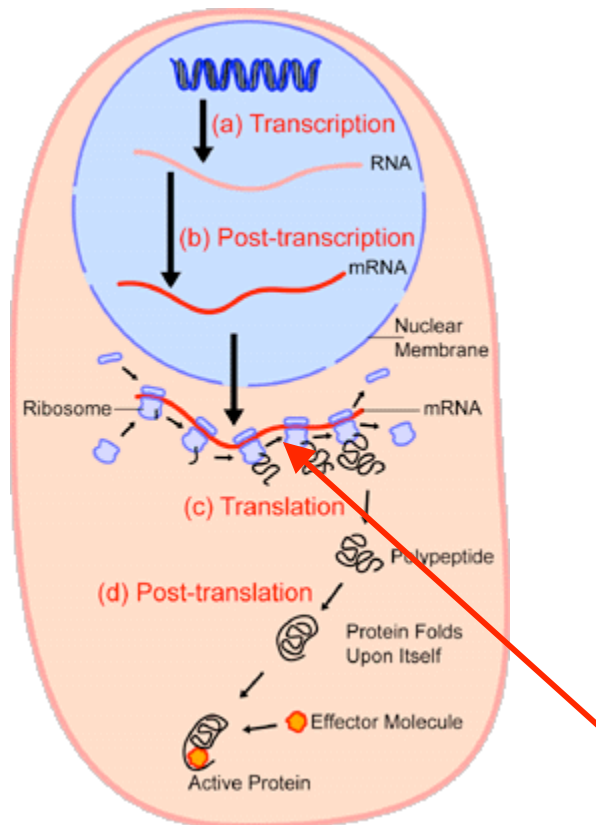
The brakes: p53 tumor suppressor

50% of the cancer is due to the damage of the genes which is related to the p53 protein production.

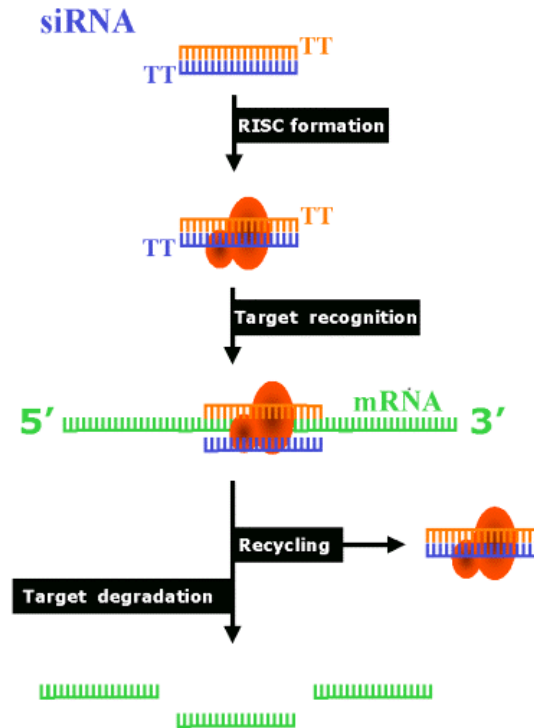




What is RNA interference?



Protein biosynthesis

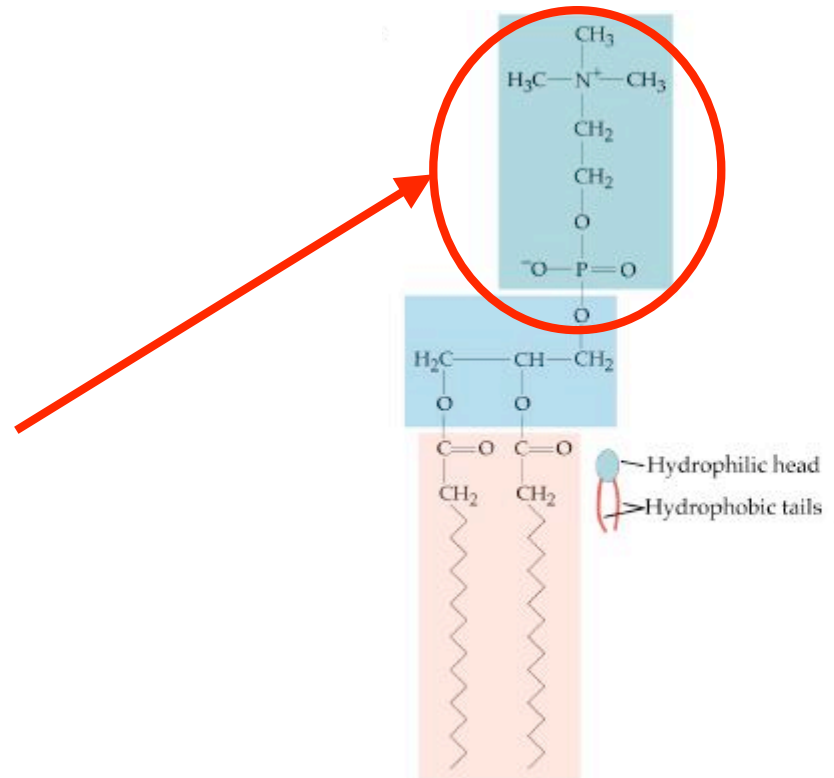
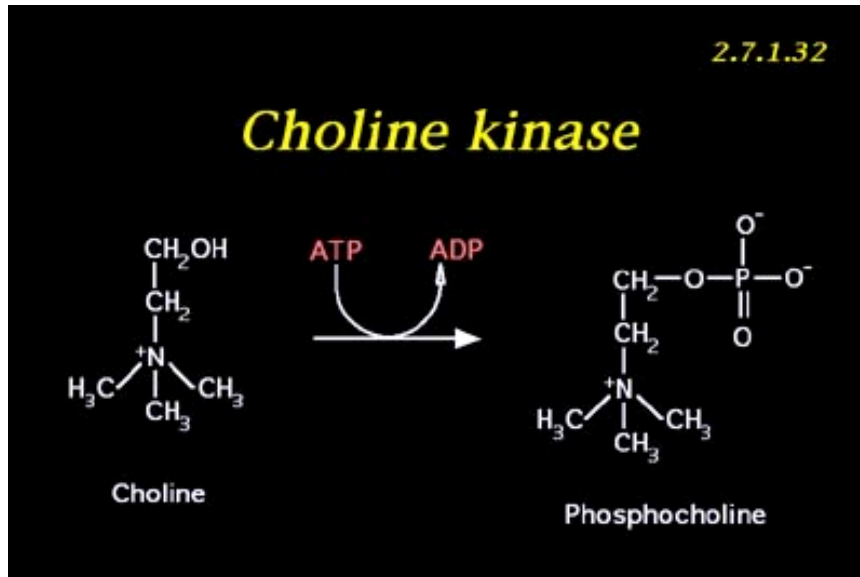


What if we add some small RNA which will form the complex and be selectively attached to mRNA and cut off them?



Choline Kinase?

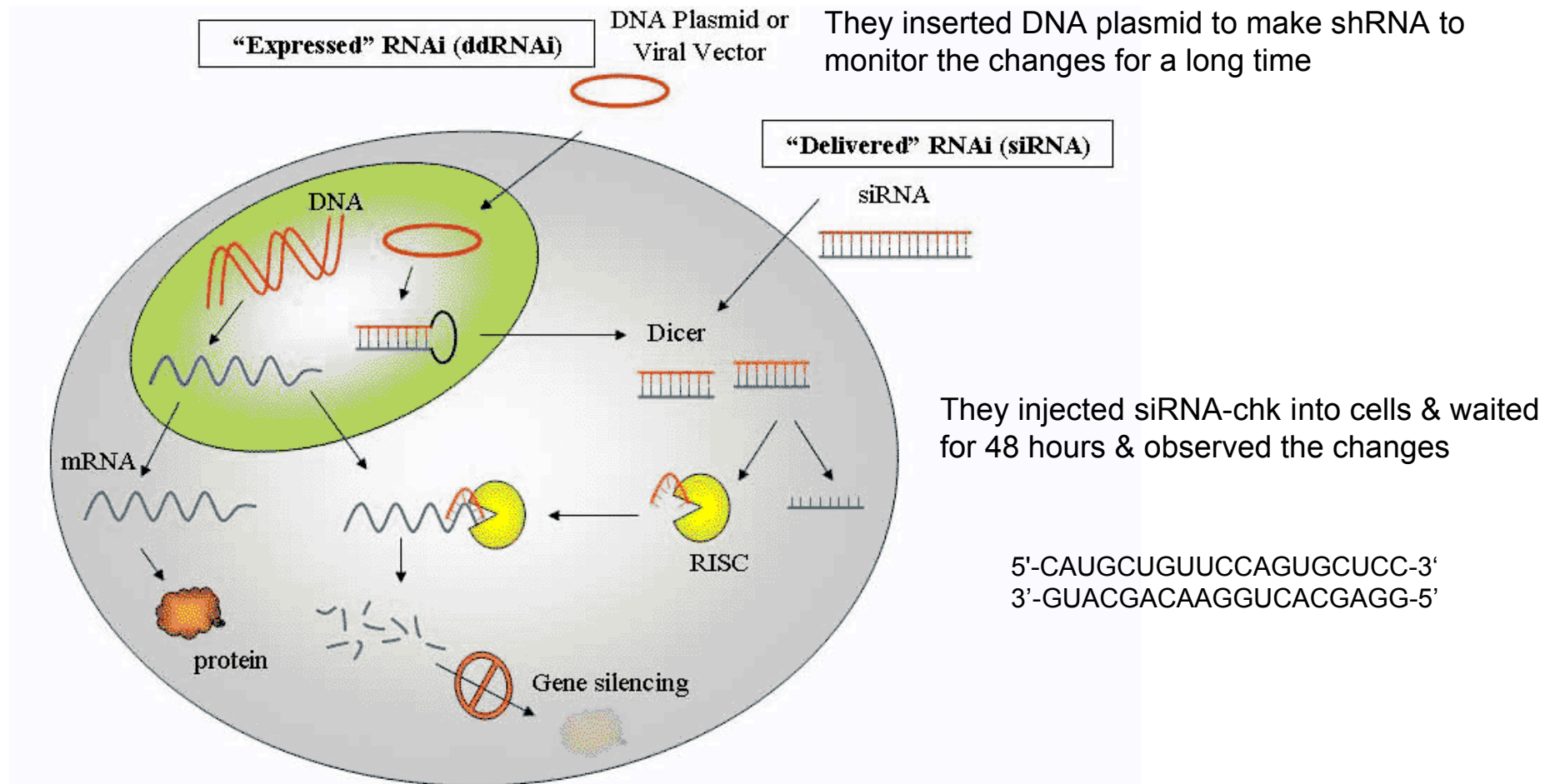
Choline Kinase increases phosphocholine



And, eventually promotes the formation of PC (phosphatidylcholine), which is one of the cancer markers

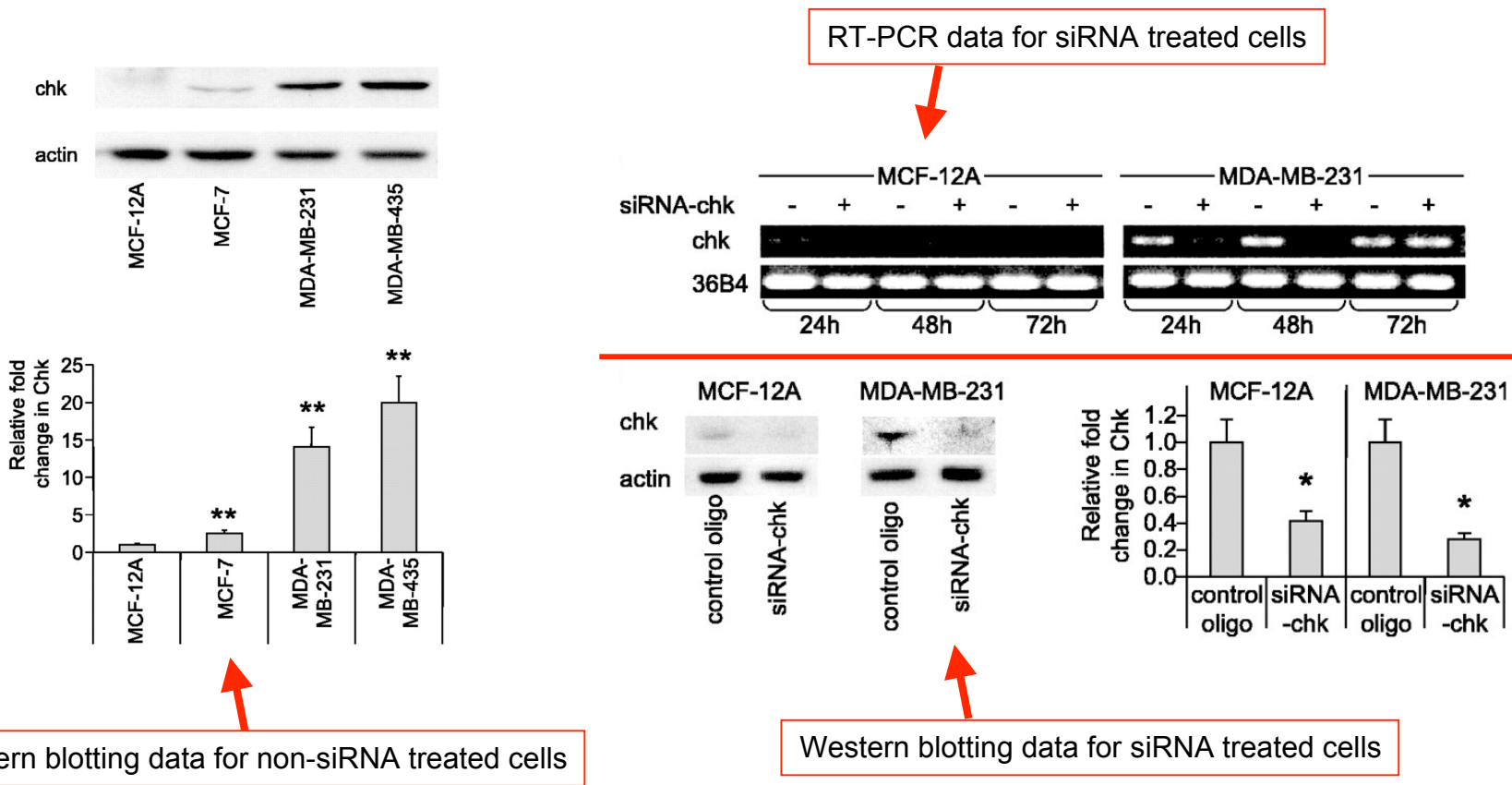


What they did?



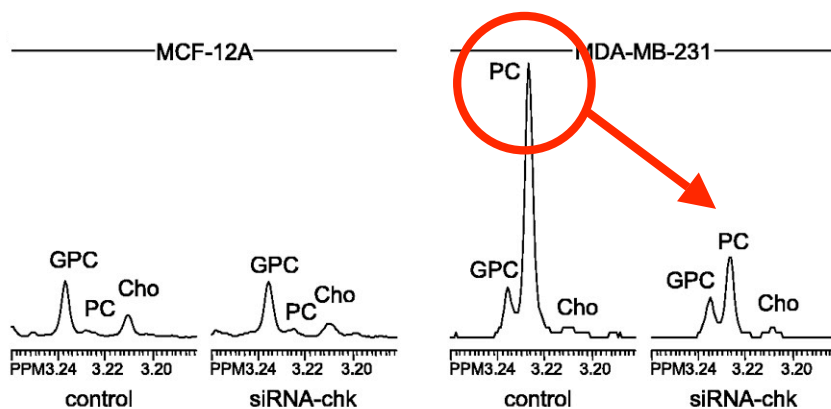


The destructive analysis - Western blotting & RT-PCR

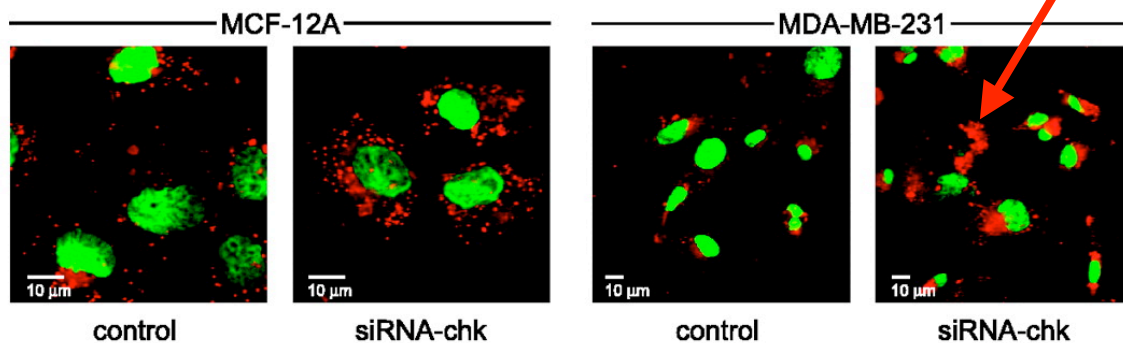




The non-destructive analysis – NMR, Immunofluorescence imaging



Lipid droplets are formed



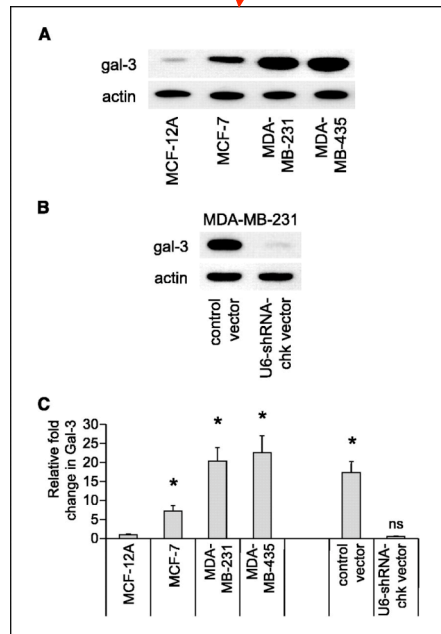


Their conclusions

RNA interference methods successfully reduced the number of choline kinase, PC & what else?

RNA interference reduced proliferation

Evidences: Marker protein Ki-67 & Marker antigen PCNA are decreased.



& RNA interference increased differentiation

Evidence: Probe protein gal-3 decreased & lipid droplets are increased.

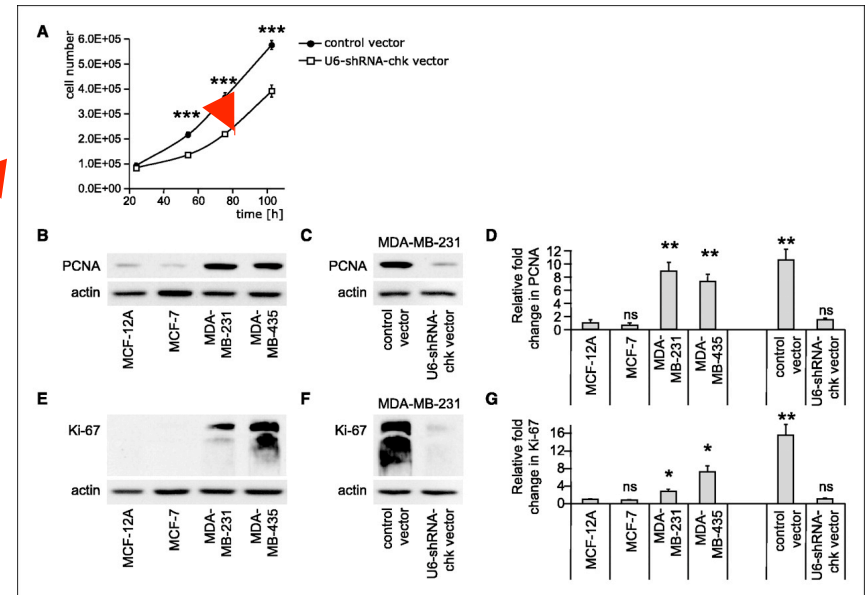
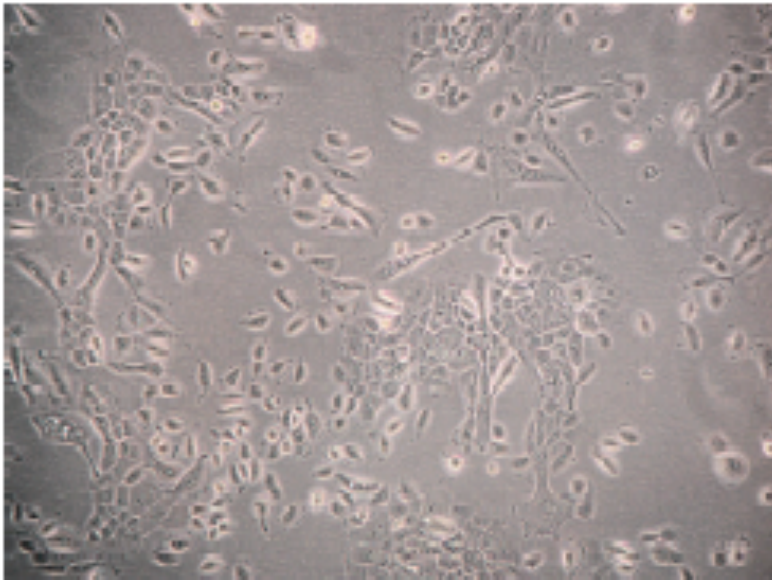
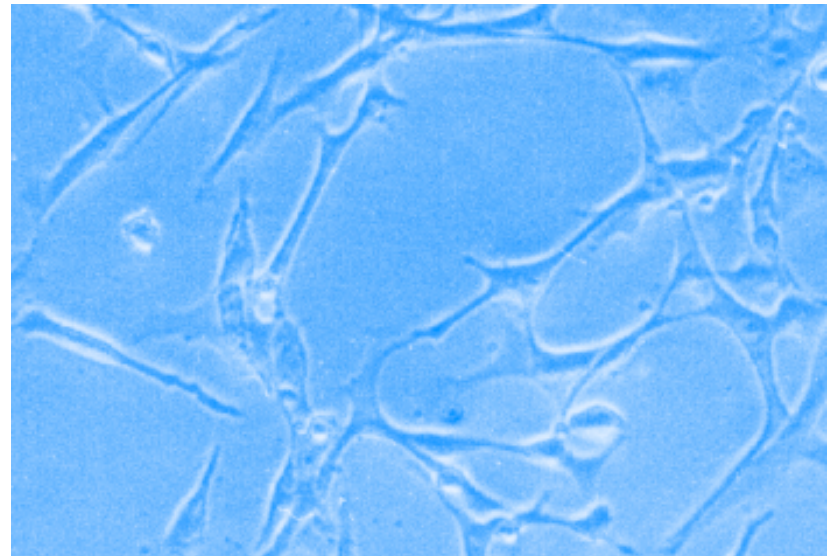




Image gallery – Normal cell vs. Cancer cells



MCF-12A (Normal breast epithelial cell)



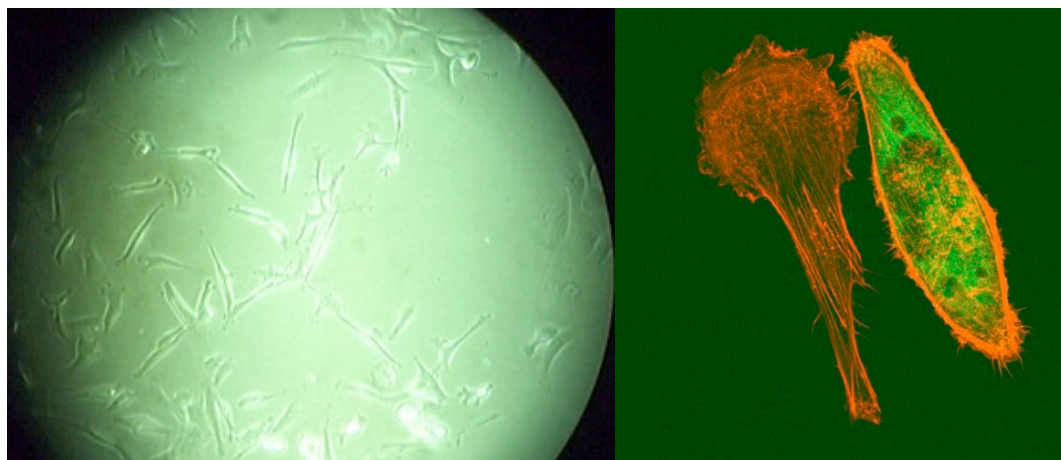
MCF-7 (weak cancer cell)



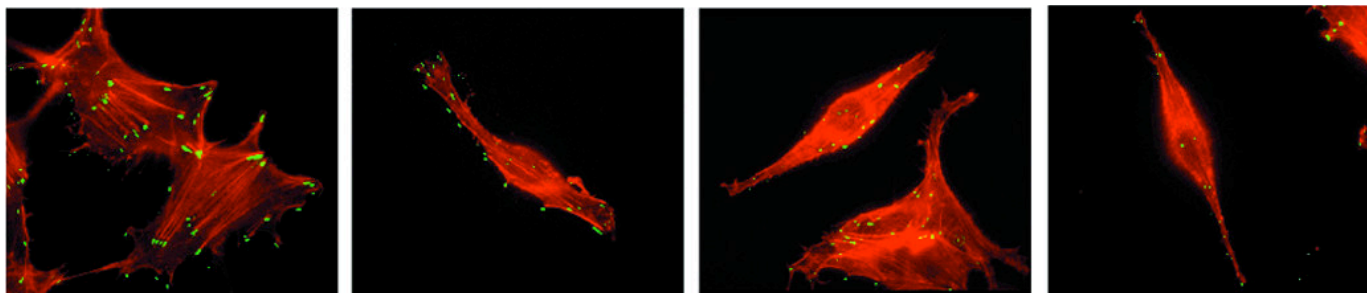
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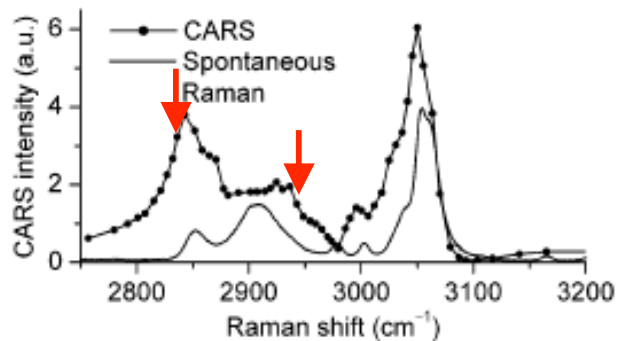
More malignant cancer cells..



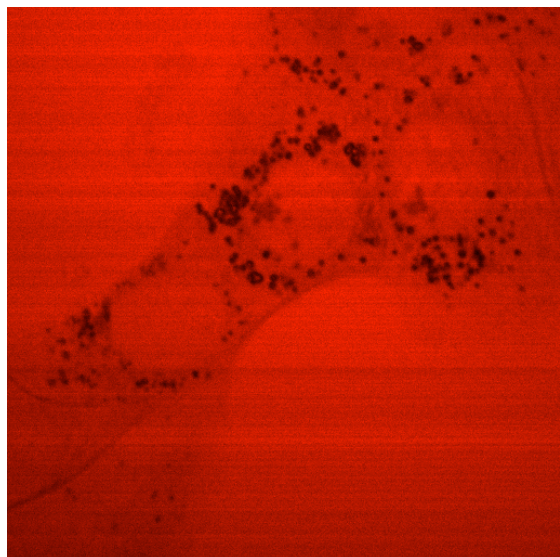
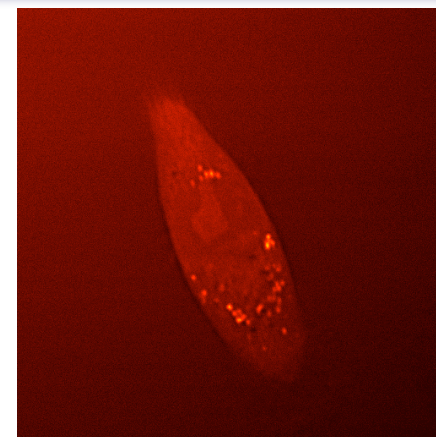
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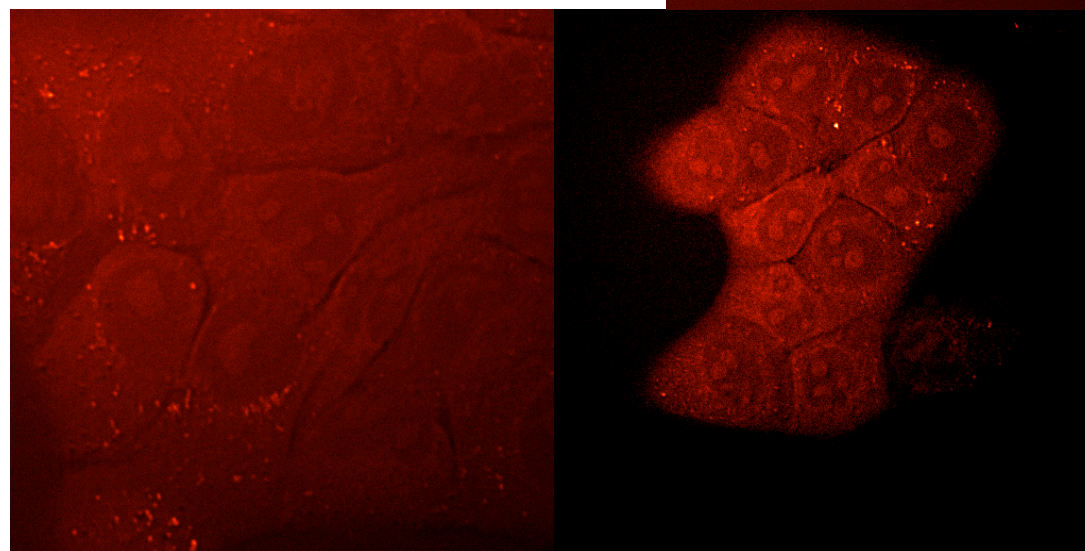
MDA-DB-435



**The very first CARS
images we got!**



$\lambda_p=810.3\text{nm} \rightarrow \text{Raman shift} = 2942\text{cm}^{-1}$



$\lambda_p=817\text{nm} \rightarrow \text{Raman shift} = 2841\text{cm}^{-1}$



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That's it!

Thanks for your patience!