

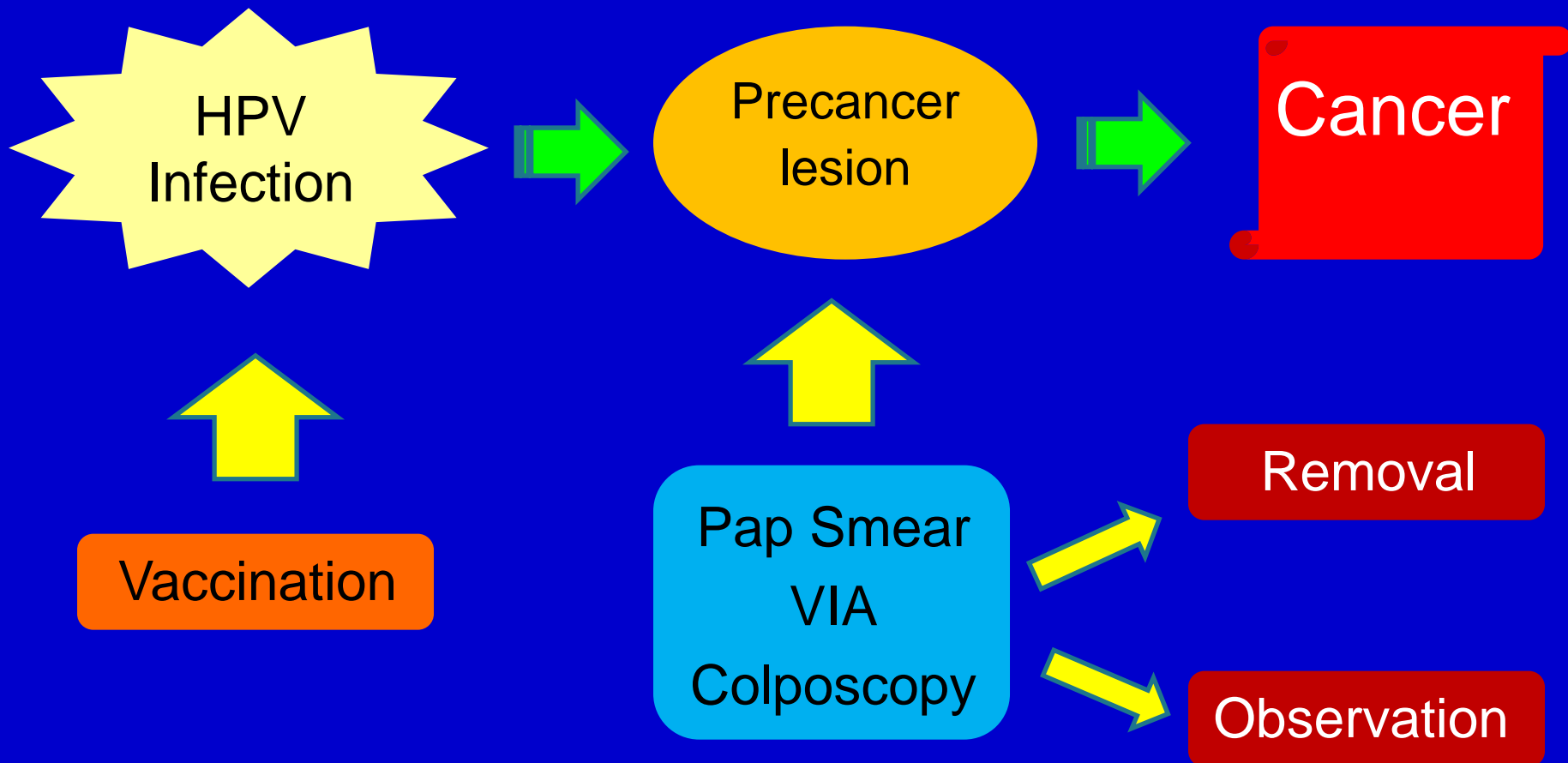
Celecoxib
as a future chemoprevention agent
by reduces proliferation, increases apoptosis
and tumor size reduction

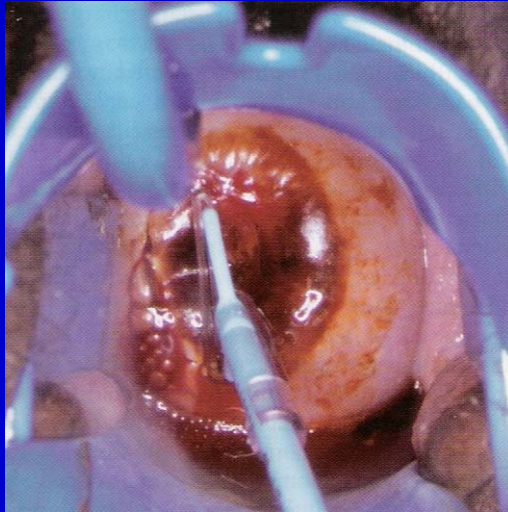


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Introduction

- Cervical cancer is a second most common and highest mortality in developing country.
- It wouldn't be improved in next few decades because of low coverage screening.
- Prevention effort should be considered for high risk people to reduced cervical cancer incidence.





Mitchell (1994): 2 year recurrence rate : 20 %

What's Next ?

Chemoprevention

CHEMOPREVENTION

The use of natural, synthetic
or biologic chemical agent
to reverse, suppress or prevent
carcinogenic progression to invasive cancer.



HPV Infection , Precancer Lesion

Chemoprevention agent

➤ Tamoxifen:

Effective for high risk, but not for healthy people

➤ Retinoid:

- Has a good chance for chemoprevention agent.

- ■ Inhibits TATA box at COX-2 promoter

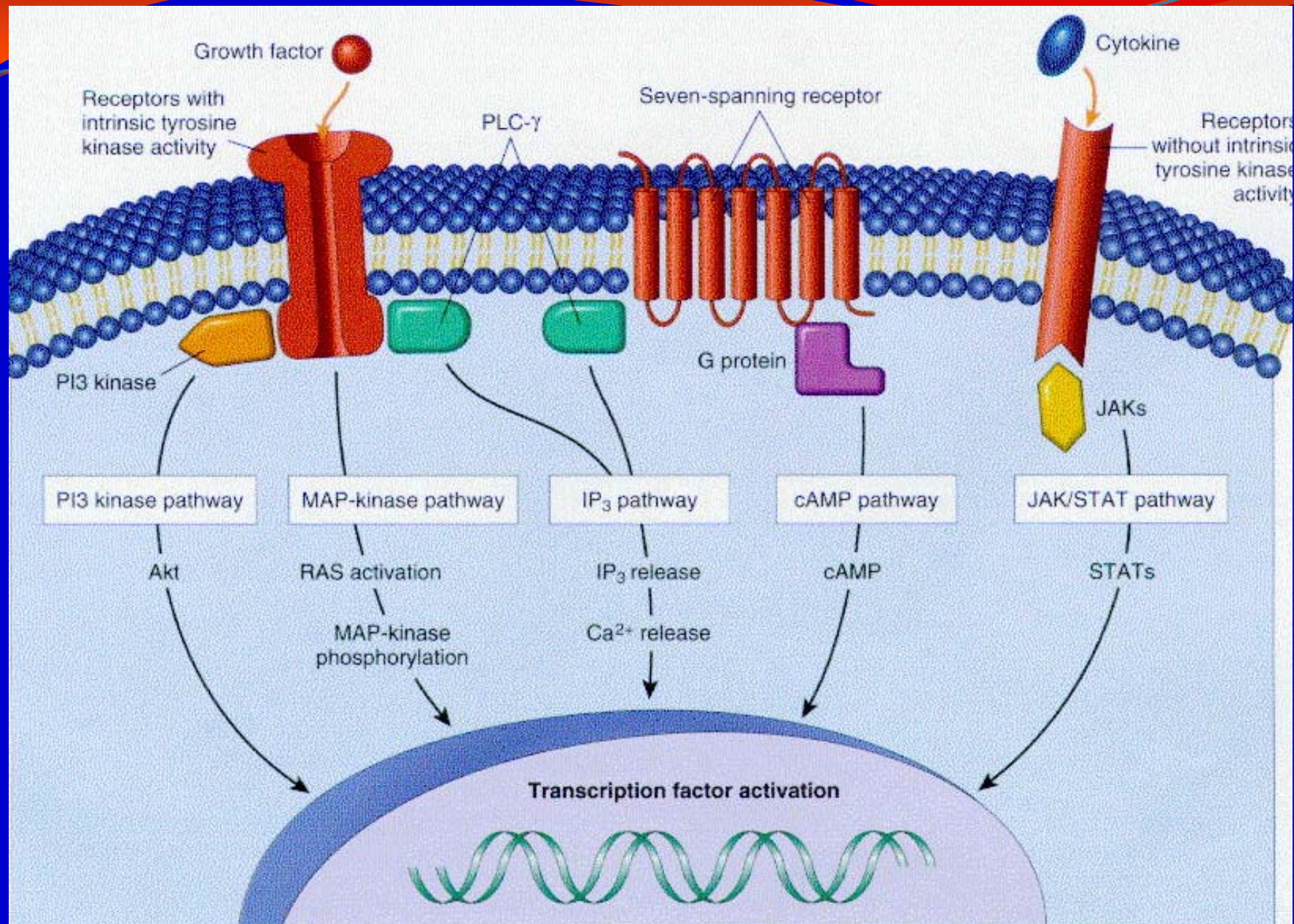
➤ NSAID

Evidences of COX-2 role on carcinogenesis.

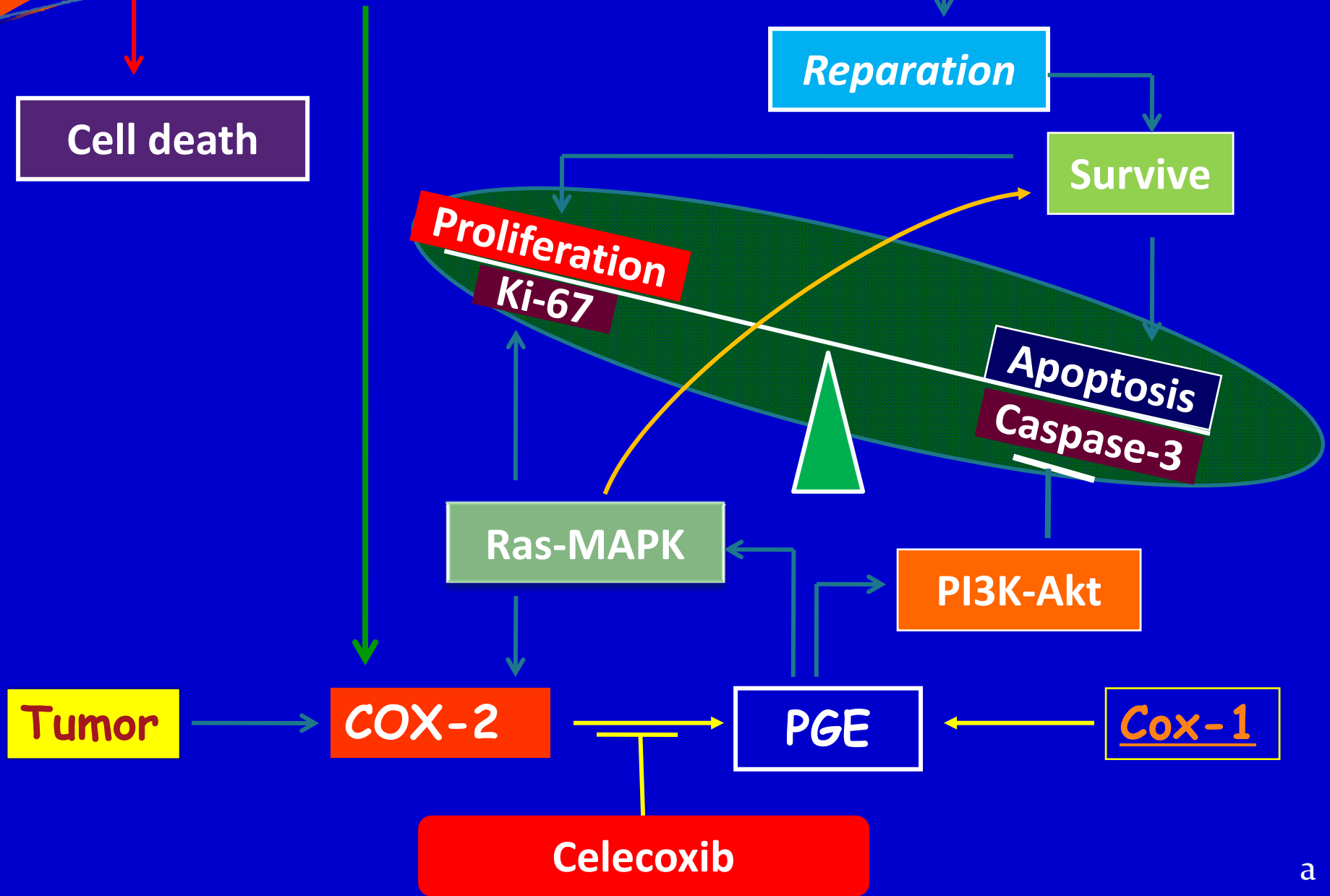
- Sulindac reduces significant number of polyp in FAP
- COX-2 is expressed in adenoma but not in normal tissue
- COX-2 derived PGE₂ activates Ras-MAPK pathway which enhances proliferation.

Our experience

- Clinical trial and pathogenesis study in late stage cervical cancer who received chemoradiation + Celecoxib administration .
- This pathogenesis can support an effort to use Celecoxib as chemopreventive agent



Chemoradiation



Cervical Cancer
Stage IB2, IIA bulky, IIB, IIIB,
IVA

Lab, Rö, EKG

Exclusion

Inclusion

Randomization

Biopsy

USG

Tumor
Size

USG

20 Pts
Ext Chemorad +
200 mg Celecoxib b.i.d

21 pts
Ext Chemorad

mRNA Cox-2
Cox-2
Caspase-3
Ki-67

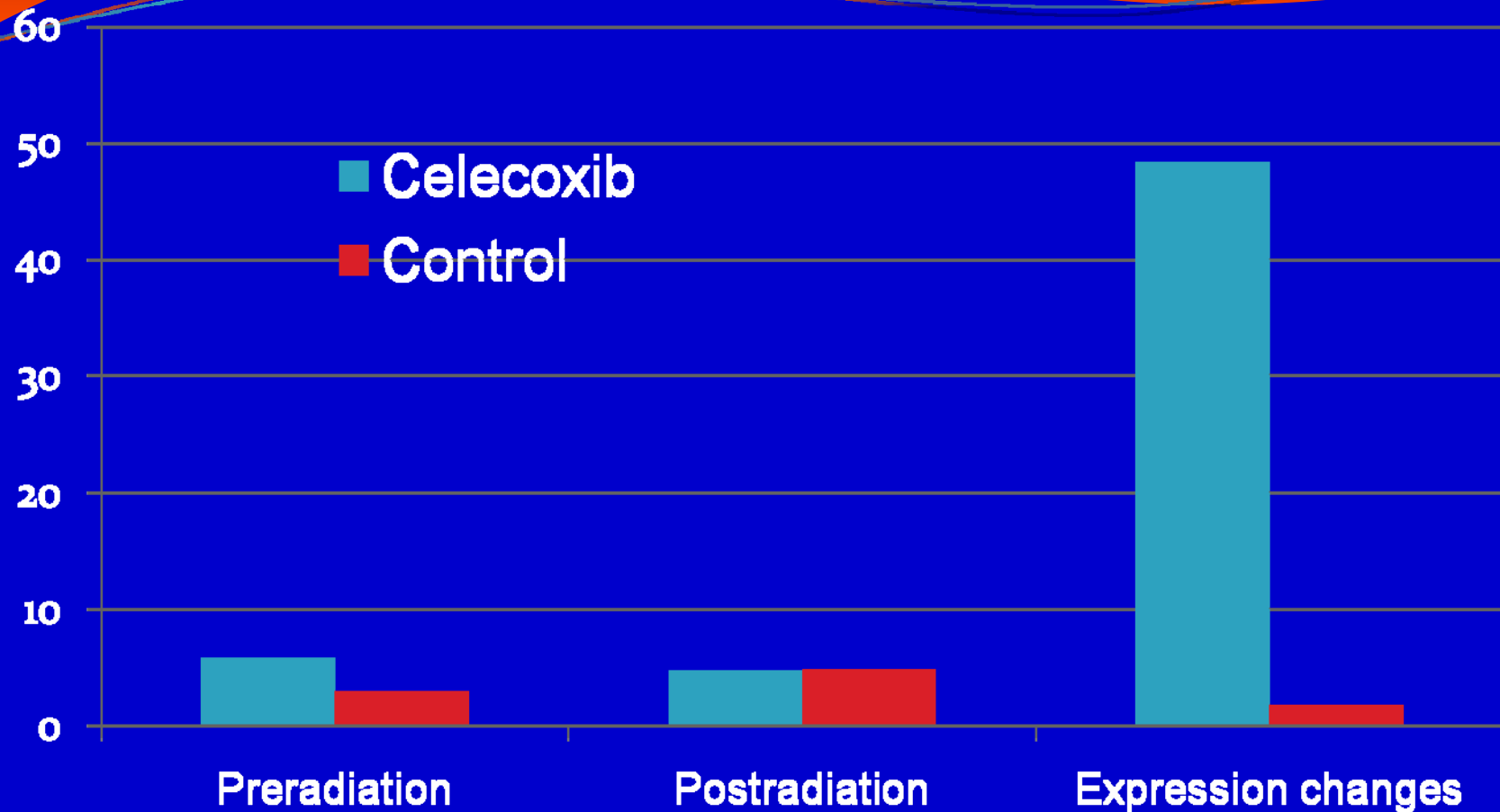
Int Chemorad

Biopsy

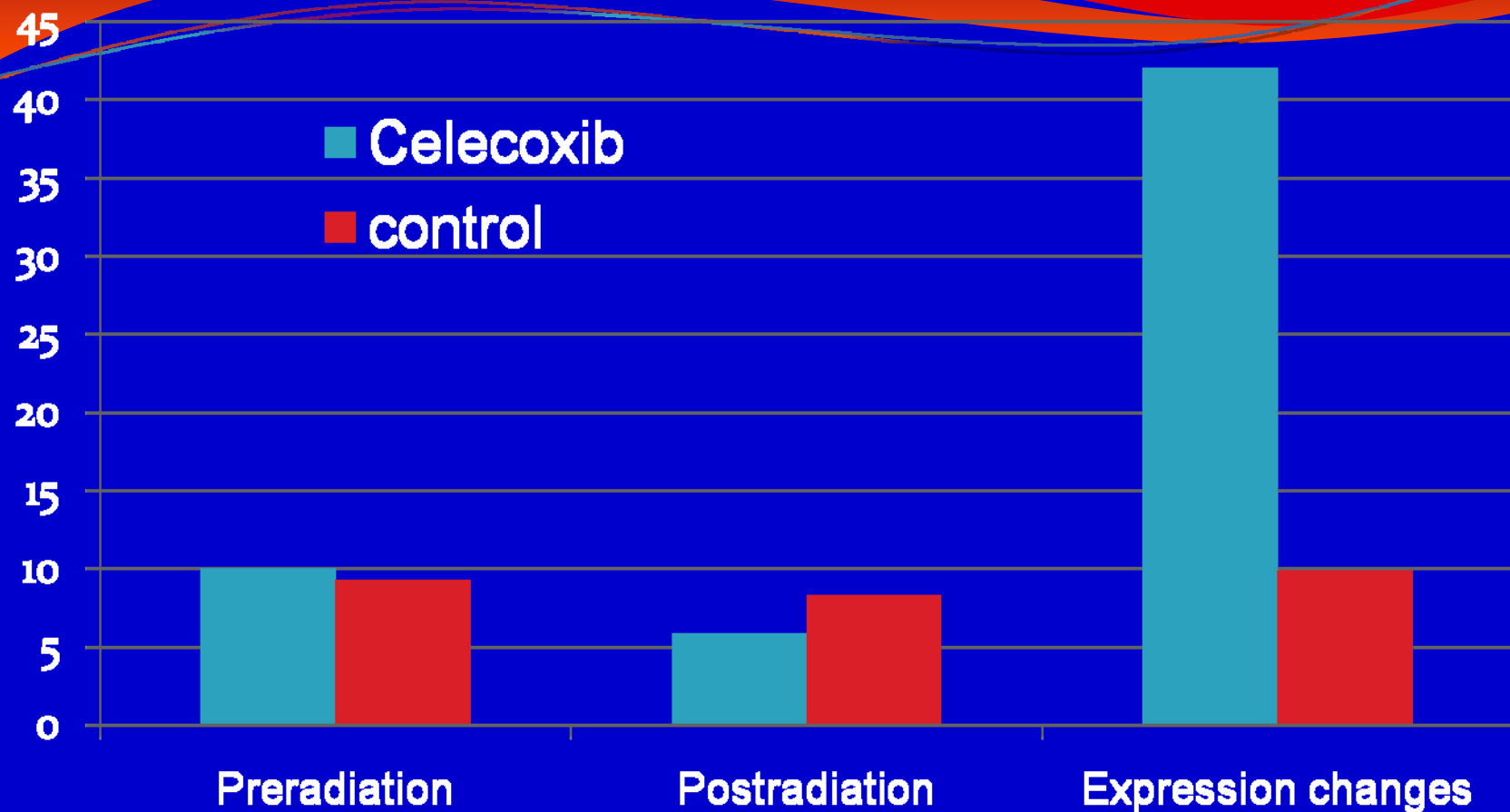
Research Protocol

Definition of parameter changes

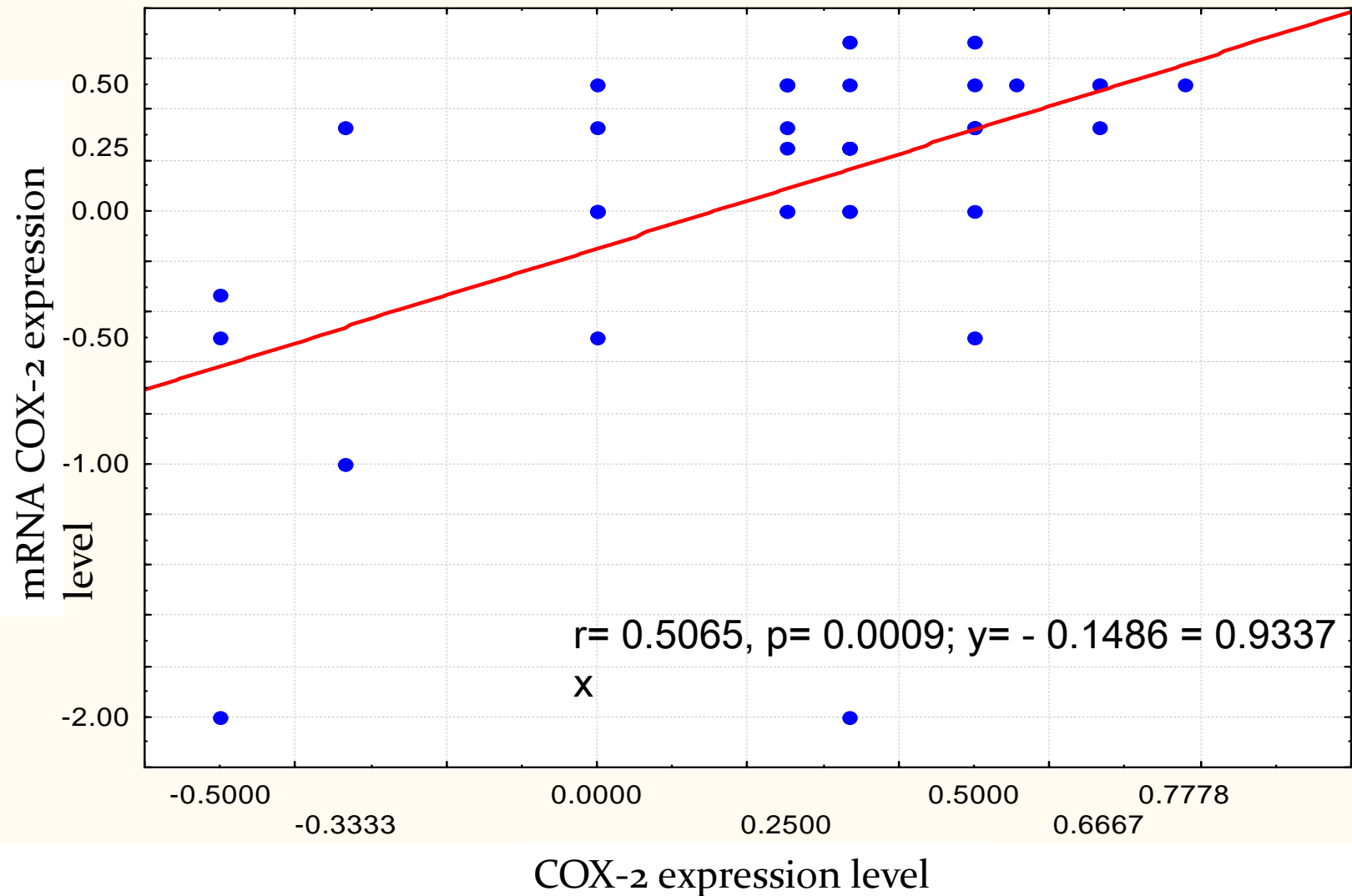
$$\begin{array}{l} \text{Expression level change} \\ \text{or} \\ \text{Tumor size reduction} \end{array} = \frac{\text{Preradiation} - \text{Postradiation}}{\text{Preradiation}}$$



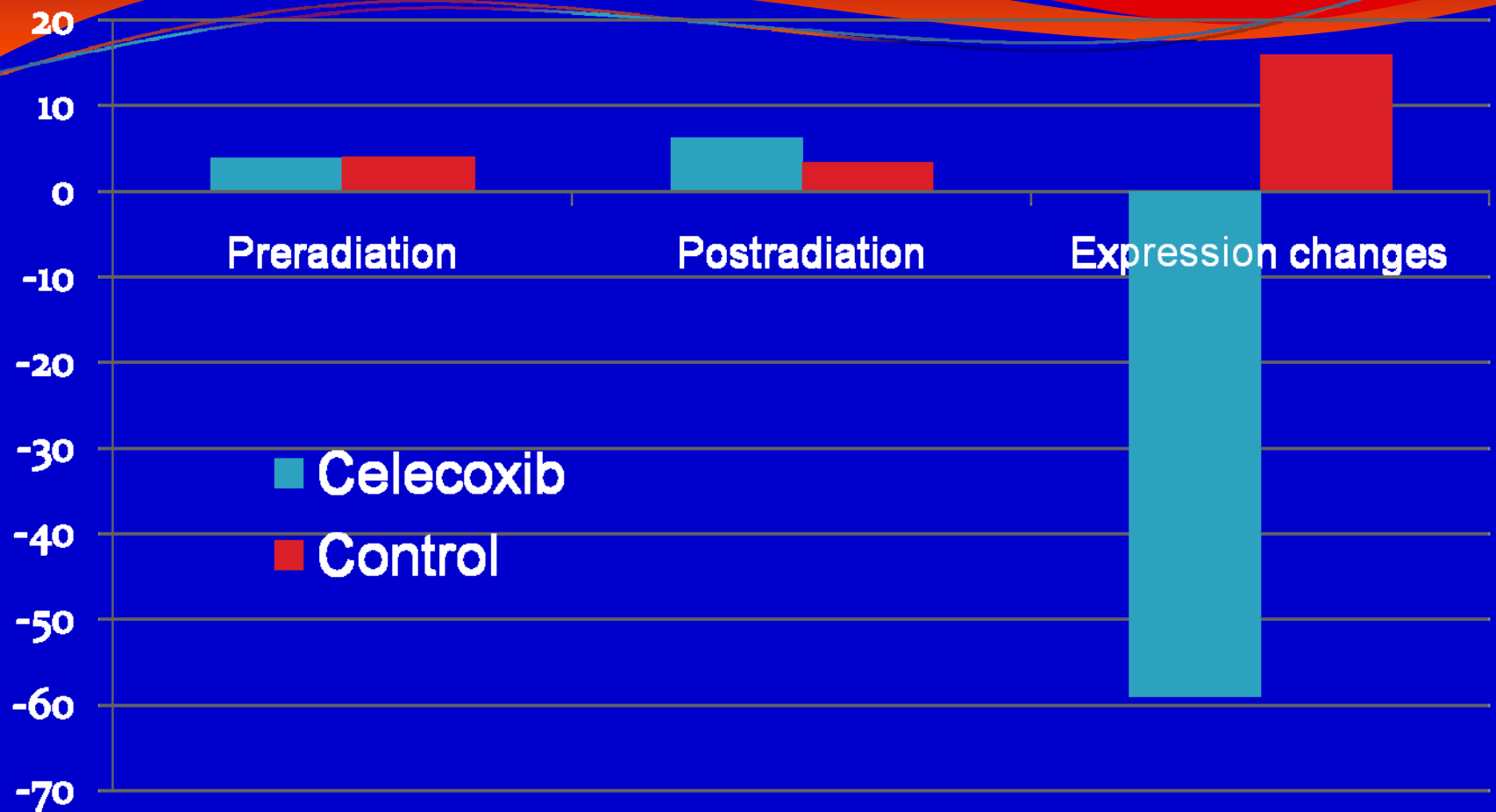
The Effect of Celecoxib administration on
mRNA COX-2 Expression Level Changes



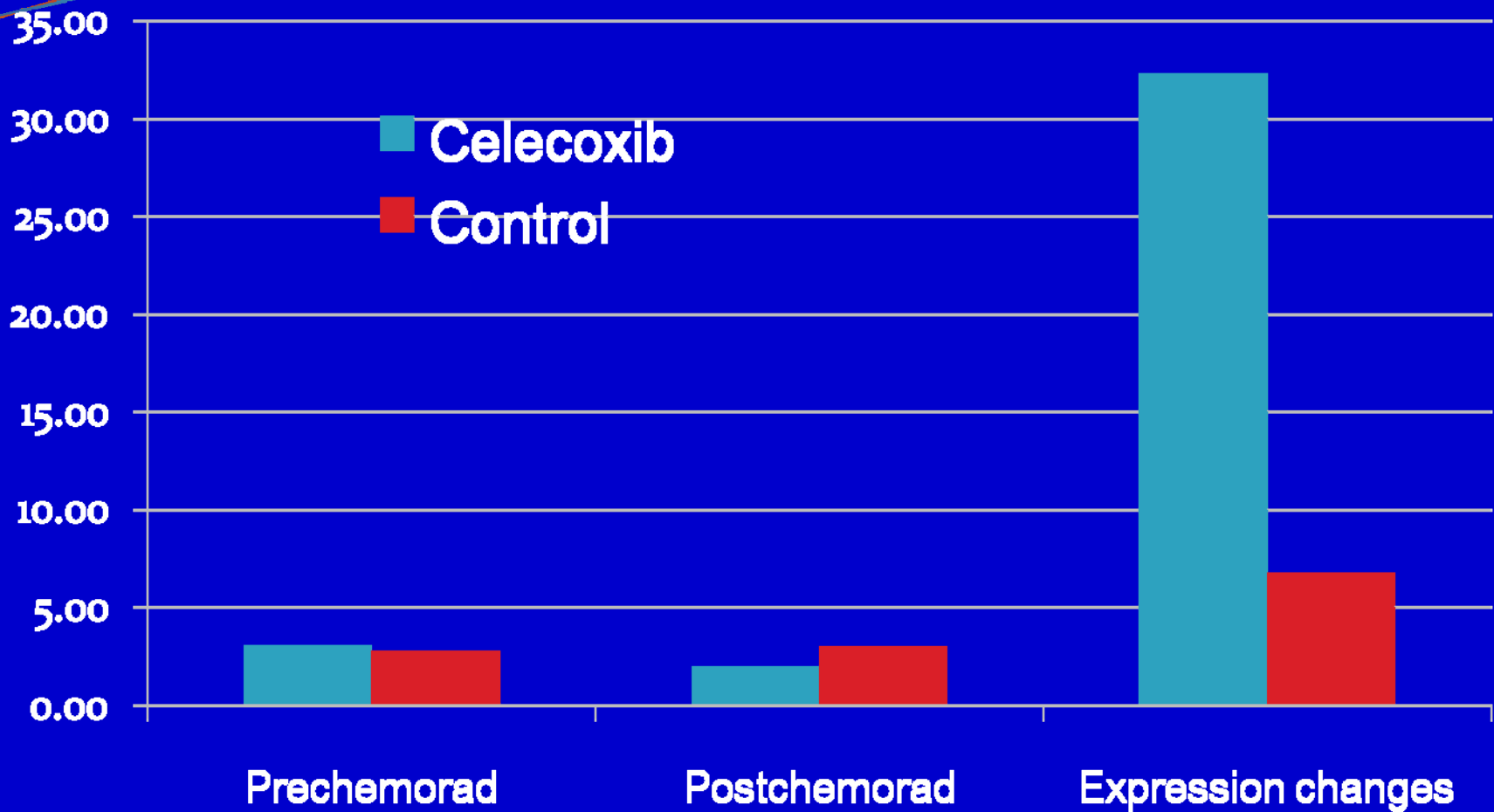
The Effect of Celecoxib administration on
COX-2 Expression Level Changes



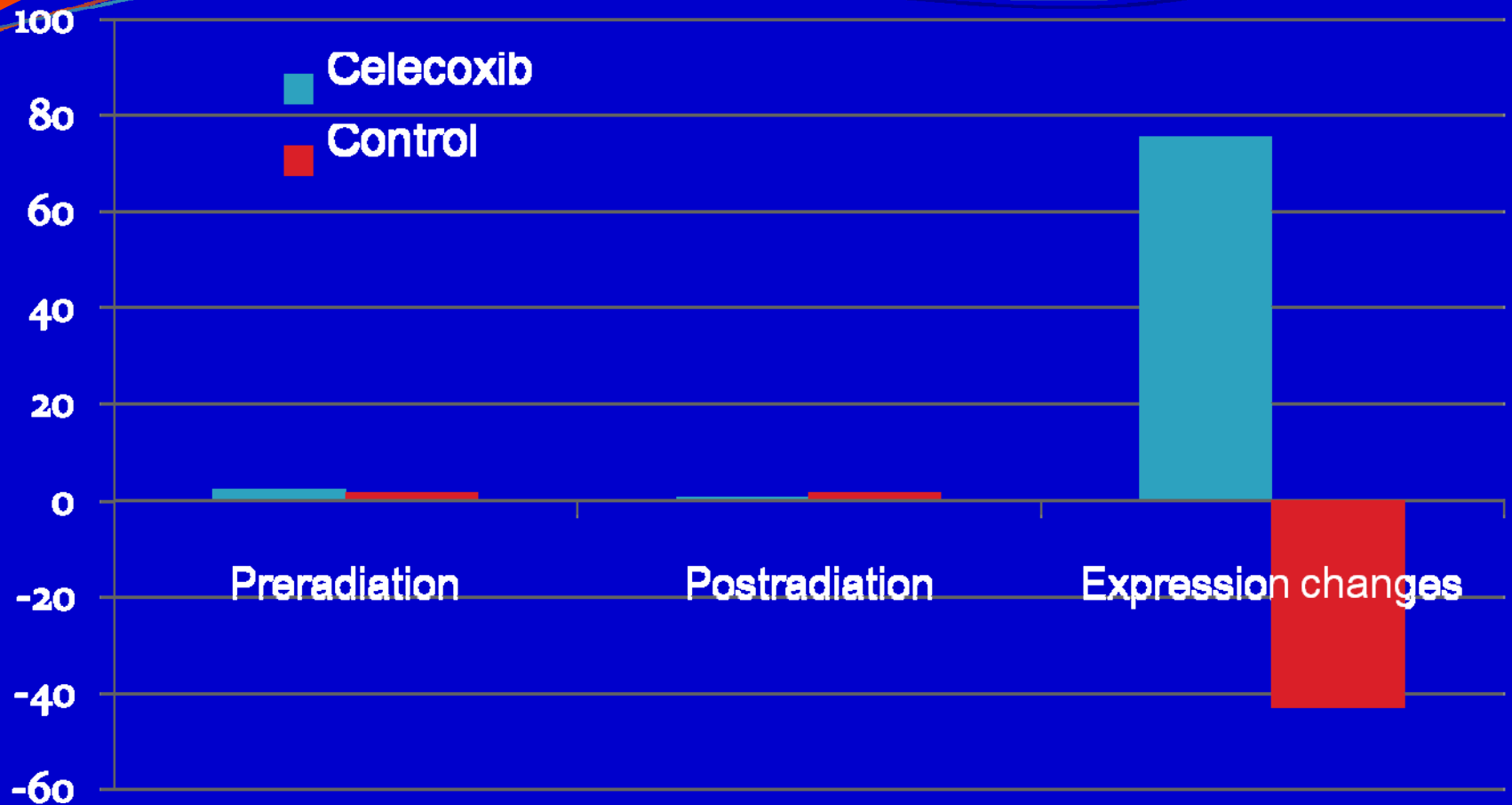
Correlation between COX-2 and mRNA COX-2 expression level



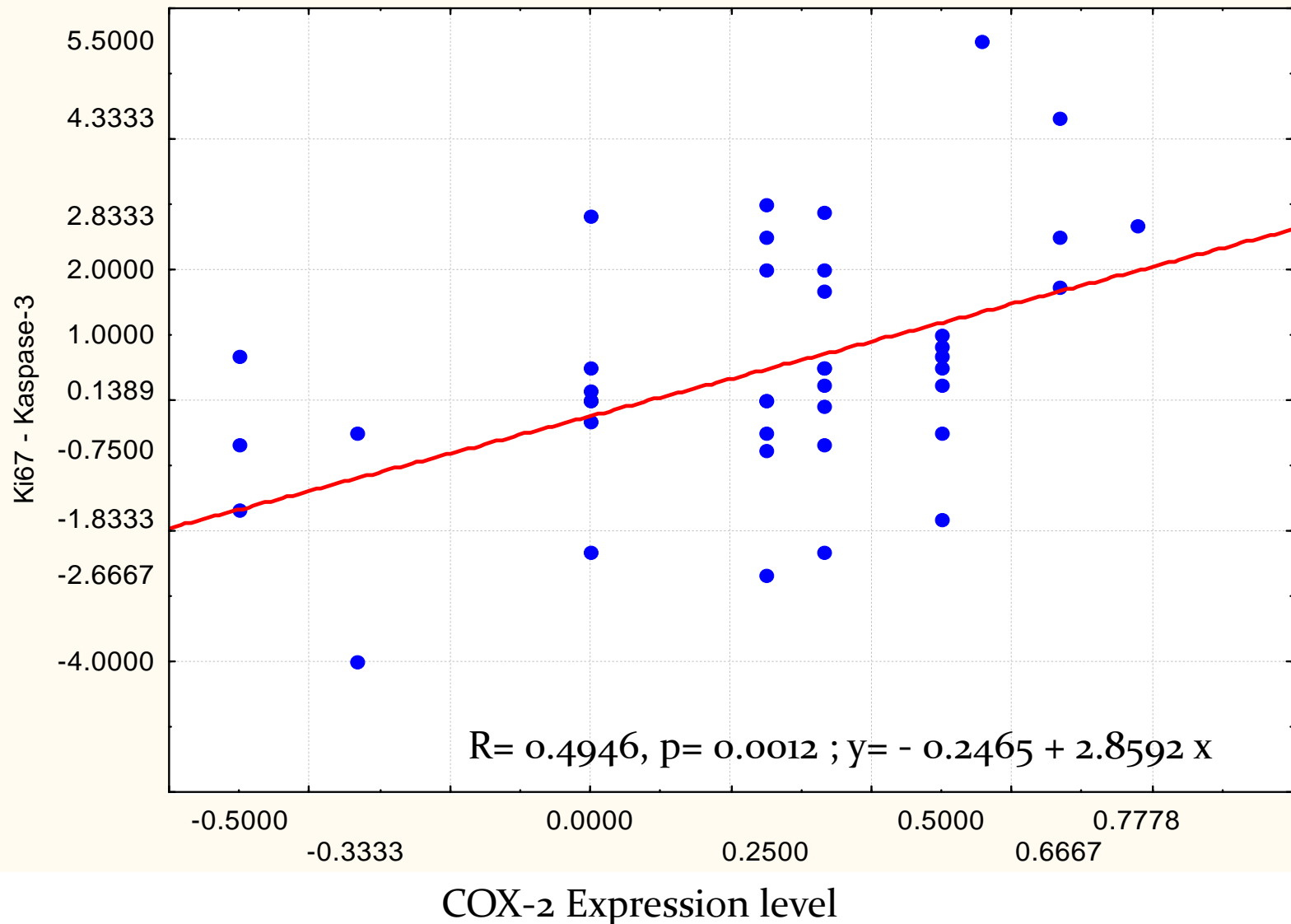
The Effect of Celecoxib administration
on Caspase-3 Expression Level Changes



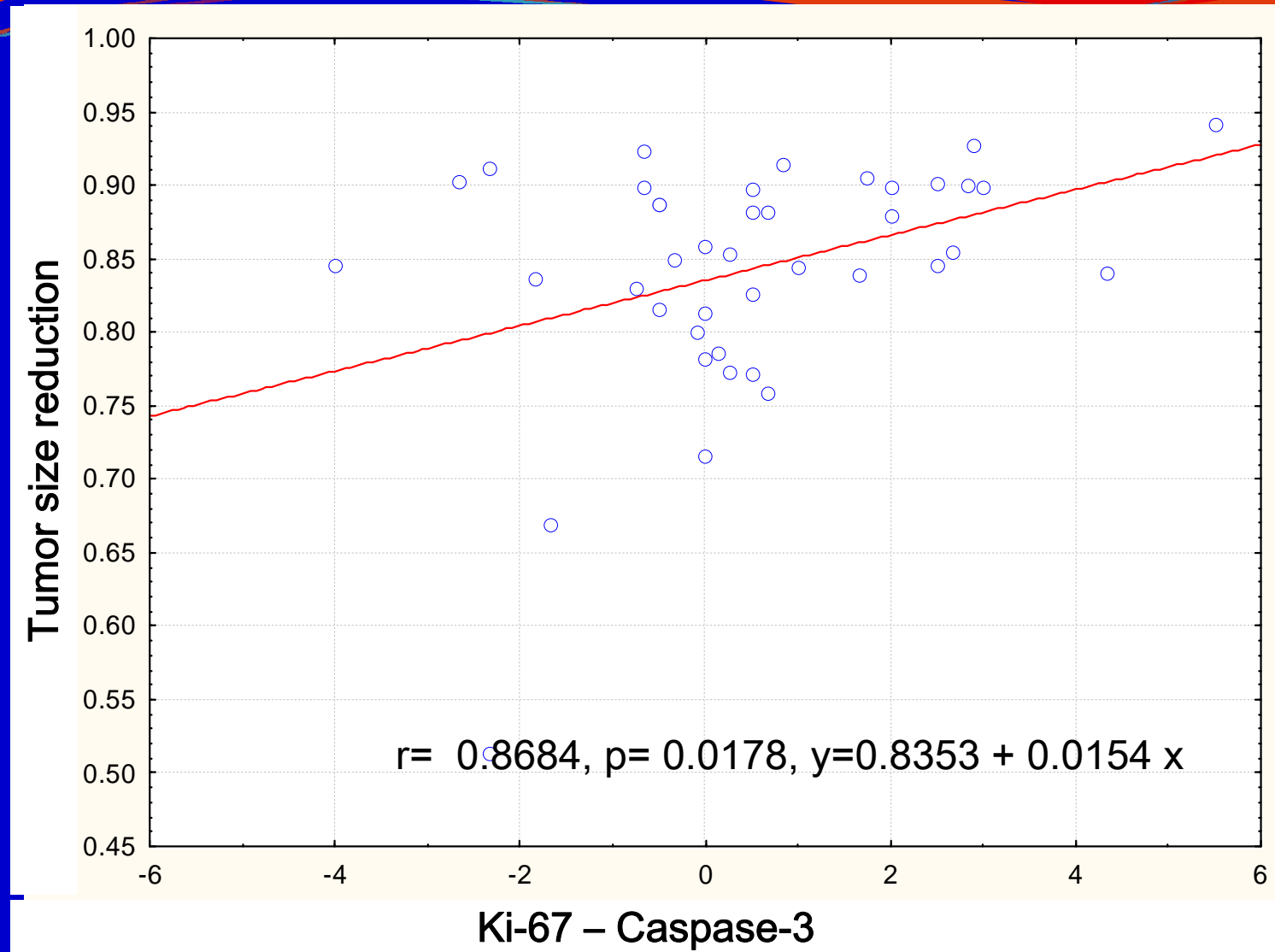
The Effect of Celecoxib Administration
on Ki-67 Expression Level Changes



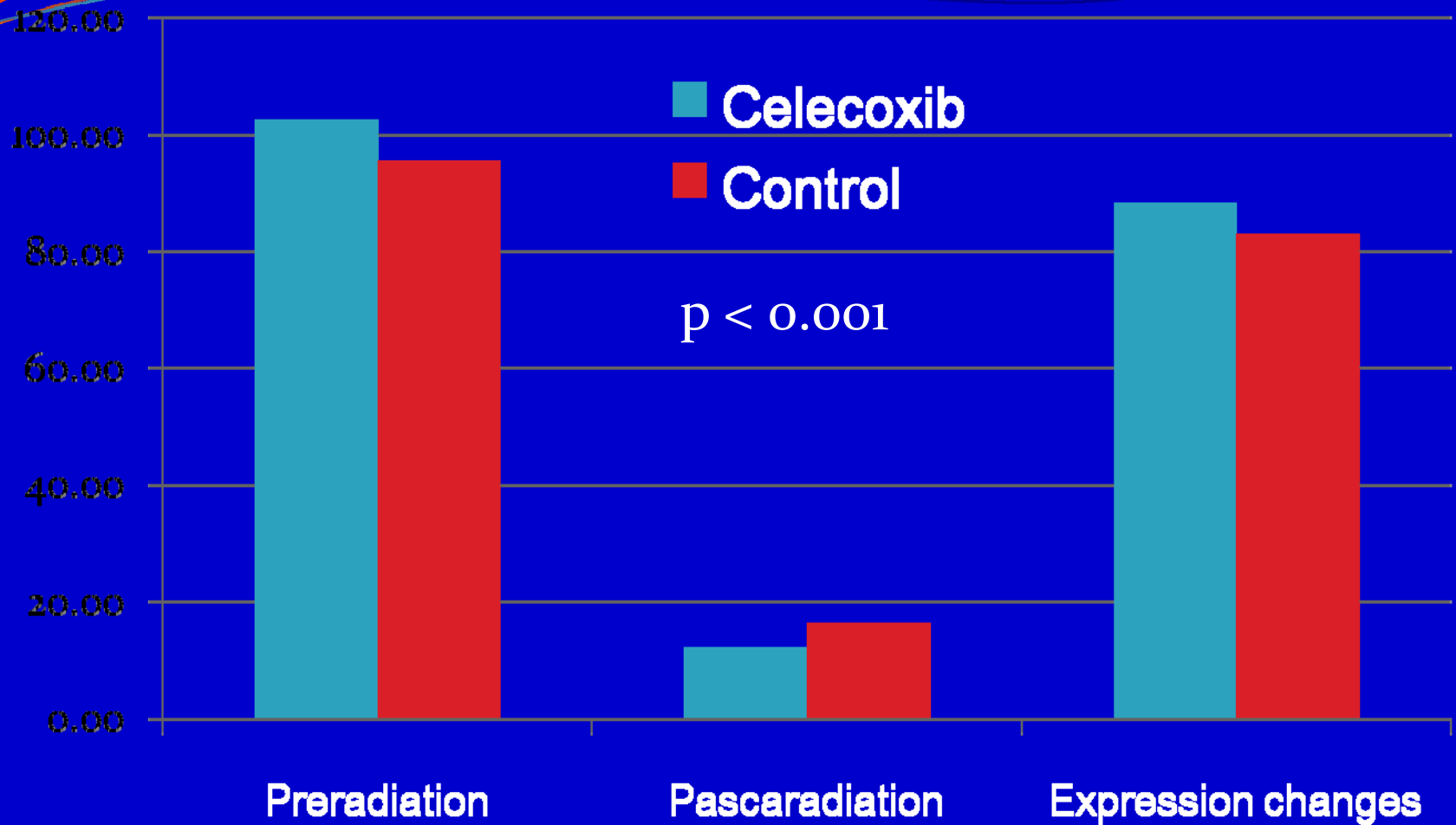
The Effect of Celecoxib Administration on
Ki-67 – Caspase-3 Expression Level Differences



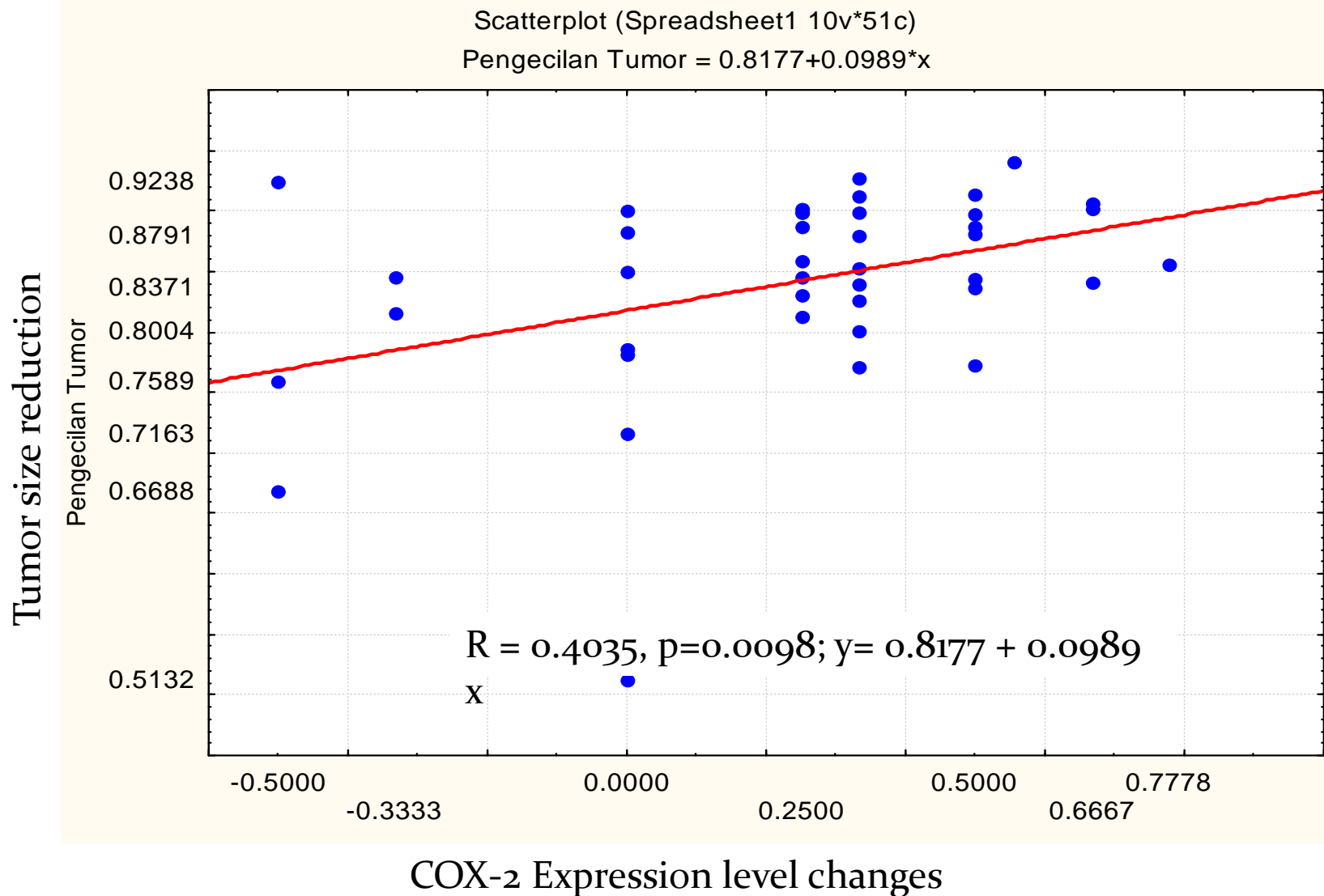
Correlation between COX-2 expression level
and Ki-67-Caspase-3 difference changes



Correlation between Ki-67-Caspase-3 differences changes and tumor size reduction



The Effect of Celecoxib Administration
on Tumor Size Reduction



Correlation between COX-2 Expression level changes and Tumor size reduction

CONCLUSION

- Chemoprevention should be considered for high risk HPV infection and precancer lesion.
- Celecoxib has a good prospect to be used as chemoprevention agent

Thank you

