Effect of the DNA synthesis inhibitor AraC on DNA double-strand breaks formation in normal and tumor cells under proton irradiation

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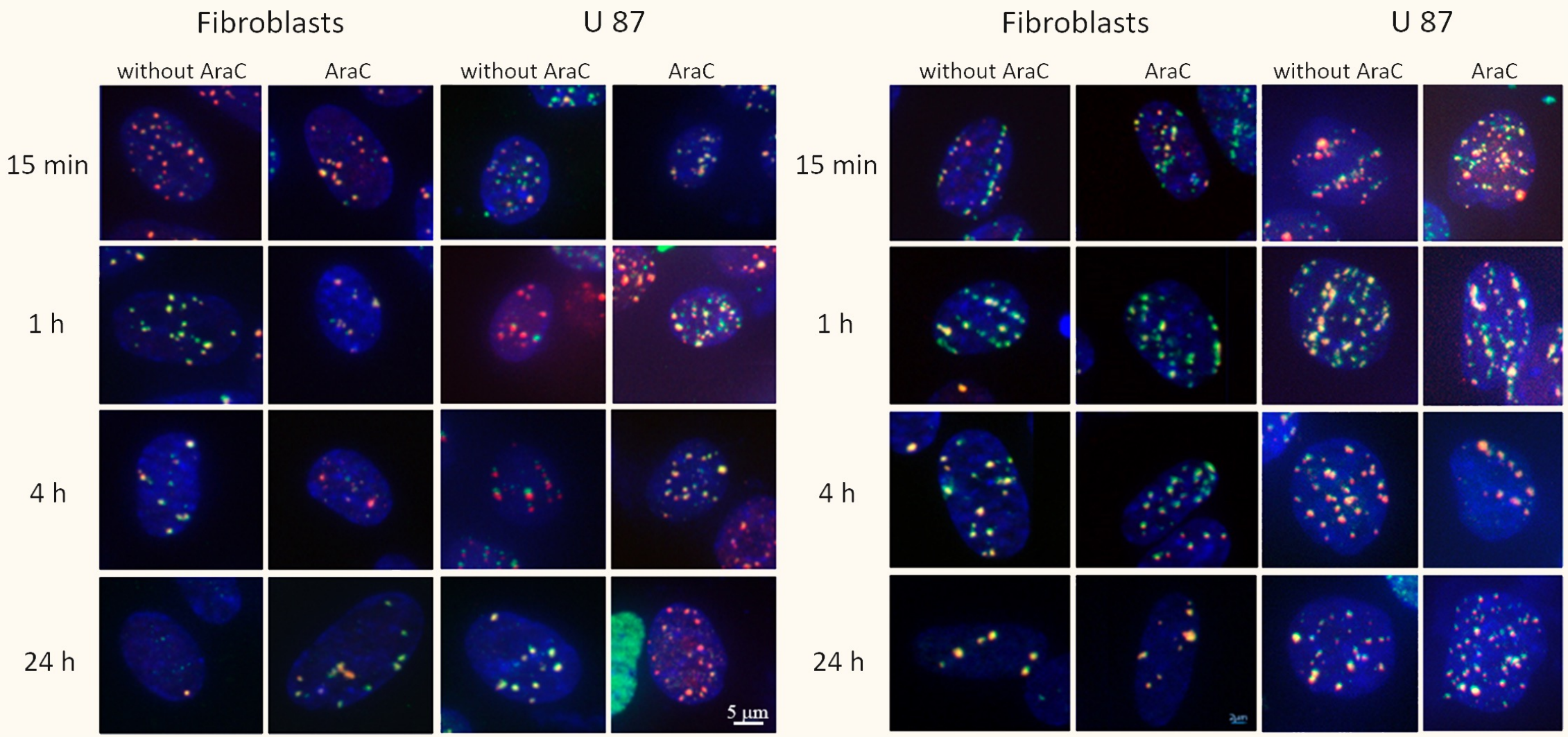
γH2AX/53BP1 foci formation and elimination (DSB repair dynamics) in normal and tumor cells



A – proton irradiation (Bragg peak), **B** - ^{15}N ions

Research goal

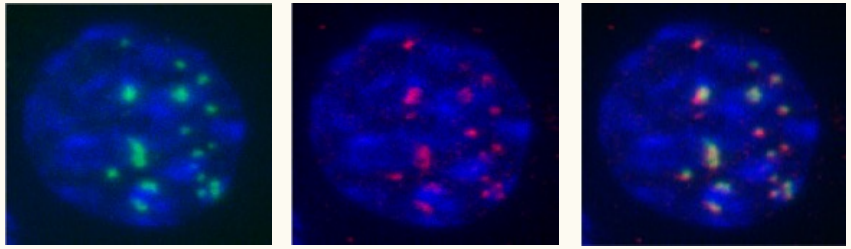
Visualization and analysis of DNA double-strand breaks (DSB) induced by protons and accelerated ^{15}N ions in human fibroblasts and U87 glioblastoma cells under the action of AraC inhibitor

Materials and methods

Type of irradiation	Energy, MeV/n	LET, keV/μm	Angle	Dose, Gy	Radiation source
Protons	150	0.25	10°	1.25	Phasotron, DLNP
^{15}N ions	14	180	10°	1.25	U-400M, FLNR

Immunostaining method

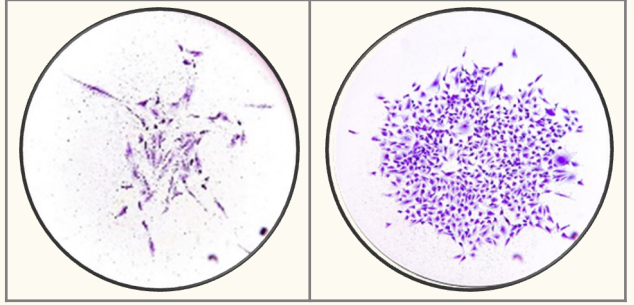
γH2AX | 53BP1 | γH2AX/53BP1



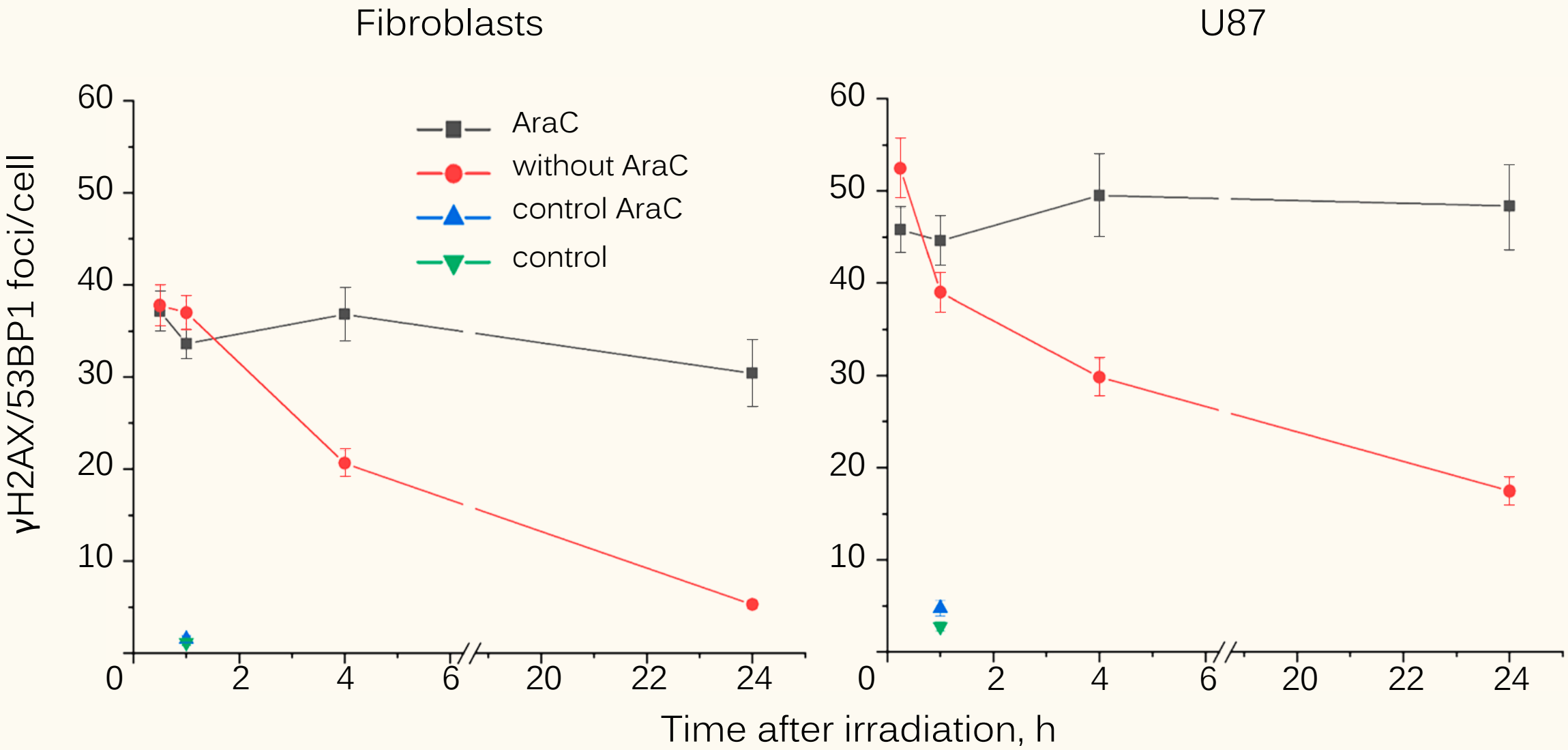
Radiation-induced foci - the site of **DSB** formation

Colony-forming unit method

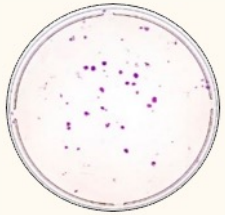
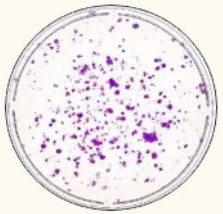
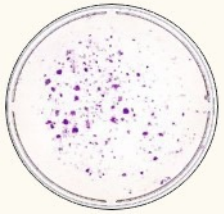
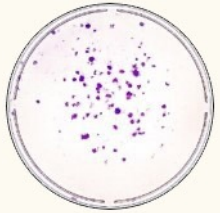
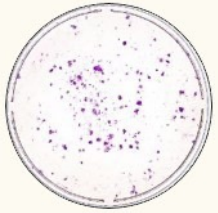
< 50 cells/colony	> 50 cells/colony

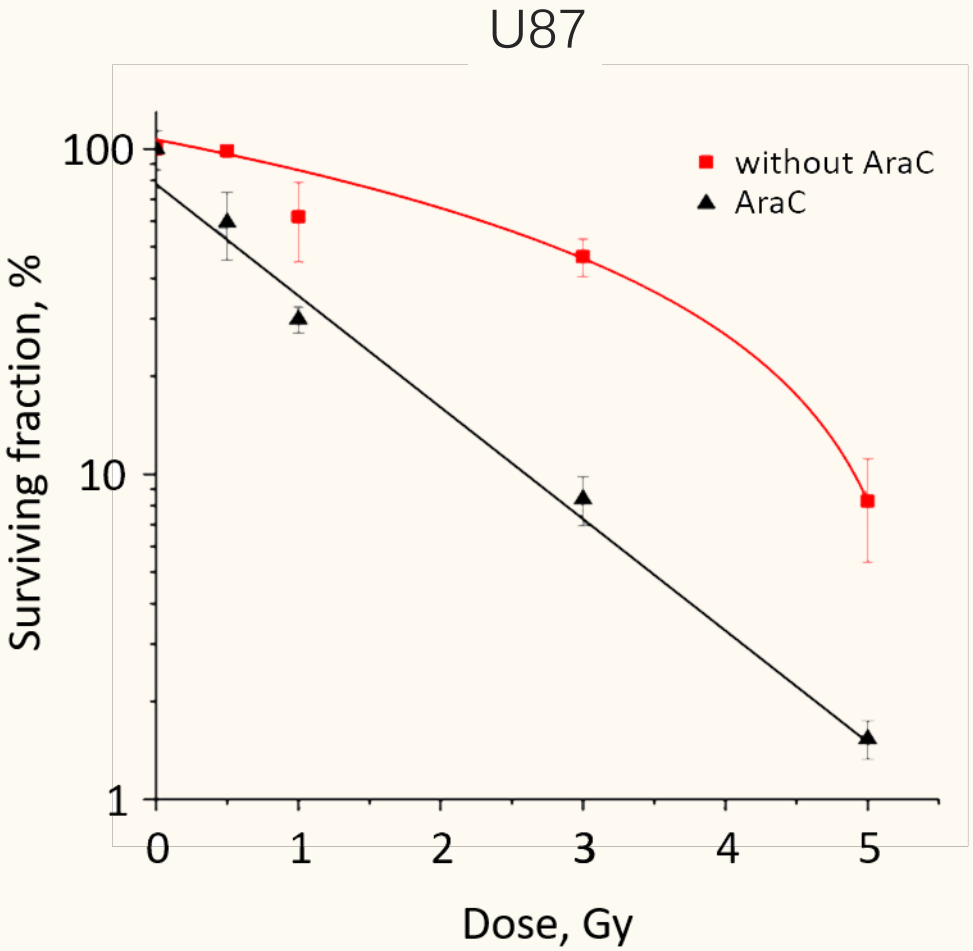


Kinetics of γH2AX/53BP1 foci formation and elimination in normal and tumor cells after proton irradiation



Survival of glioblastoma cells after exposure to protons

	Control 200 cells/plate Colonies: 35	3 Gy 2000 153	5 Gy 5000 69
without AraC			
	Control 400 cells/plate Colonies: 66	3 Gy 5000 71	5 Gy 10000 28
AraC			



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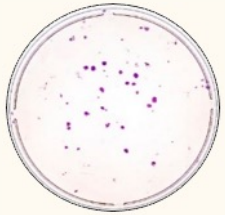
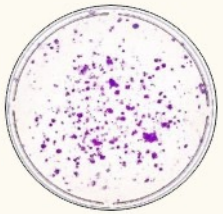
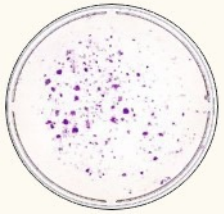
without AraC			
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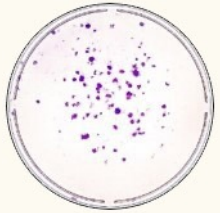
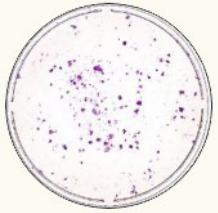
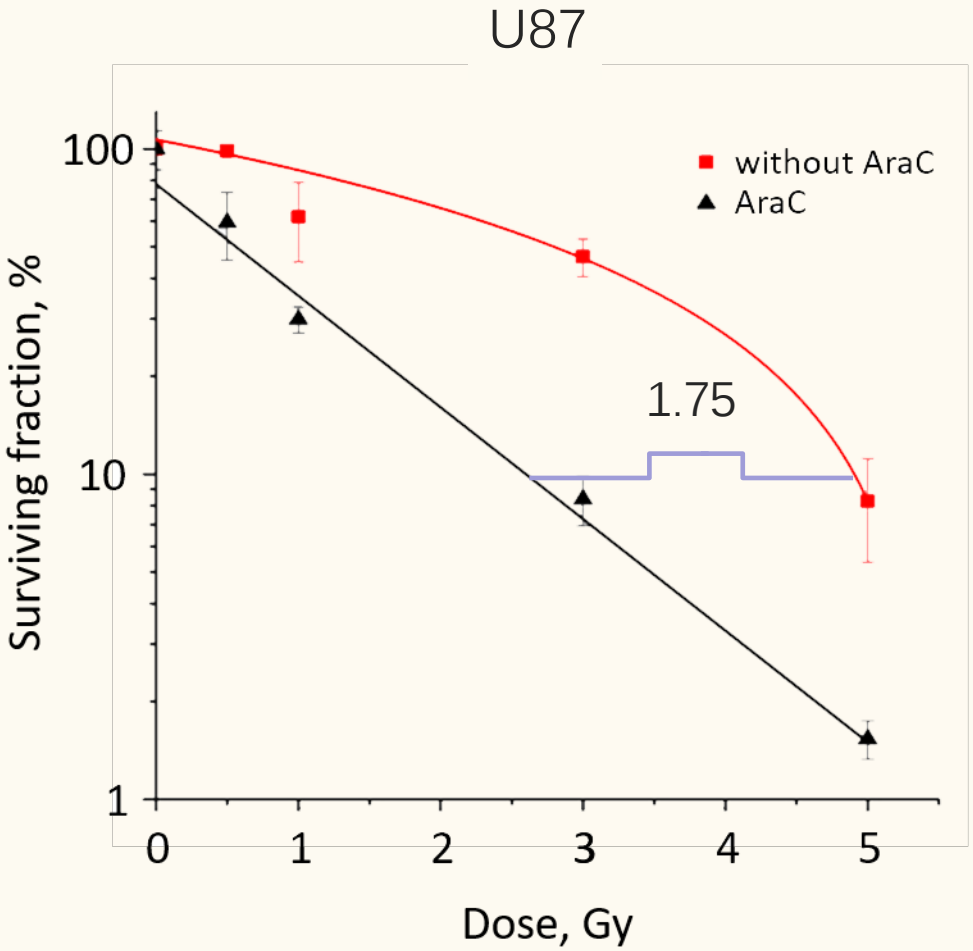
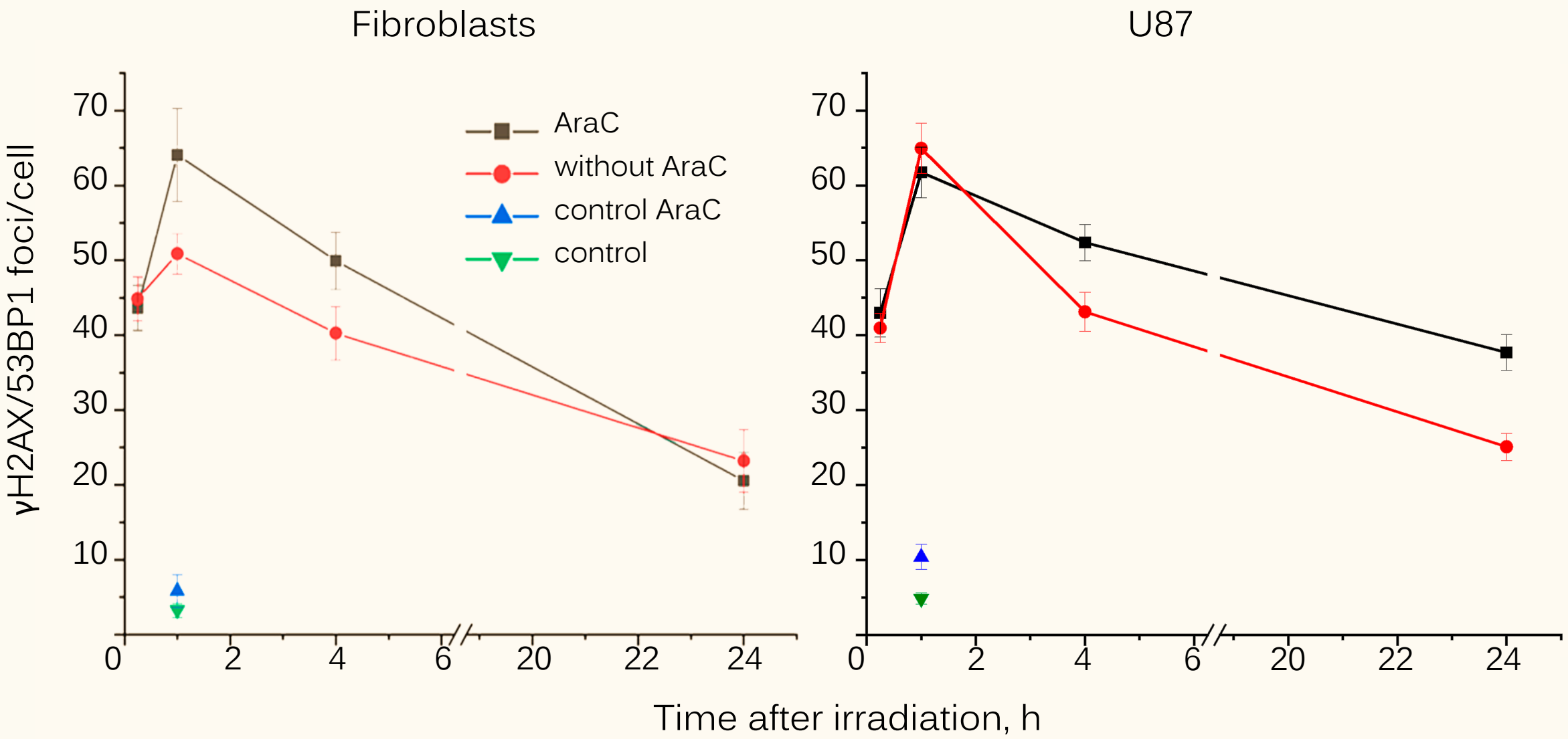
AraC			



Kinetics of γH2AX/53BP1 foci formation and elimination in normal and tumor cells after nitrogen ions irradiation



Summary

- The number of foci per cell decreases with time after proton irradiation in both types of cell cultures
- The presence of the AraC inhibitor induces an increase of a persistent foci number till the 24 h: 6-fold higher growth in the fibroblasts and 3-fold higher in the glioblastoma cells compared to the number of foci in cells that were not preincubated with inhibitor
- Colony survival of glioblastoma cells in the presence of AraC upon proton irradiation is significantly reduced
- It was shown that upon irradiation with accelerated ^{15}N ions, the kinetics of DNA DSB repair in fibroblasts is successfully carried out both under normal conditions and under the influence of the AraC inhibitor

thank you for your attention!