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Cellular therapy treatment of radiation cystitis

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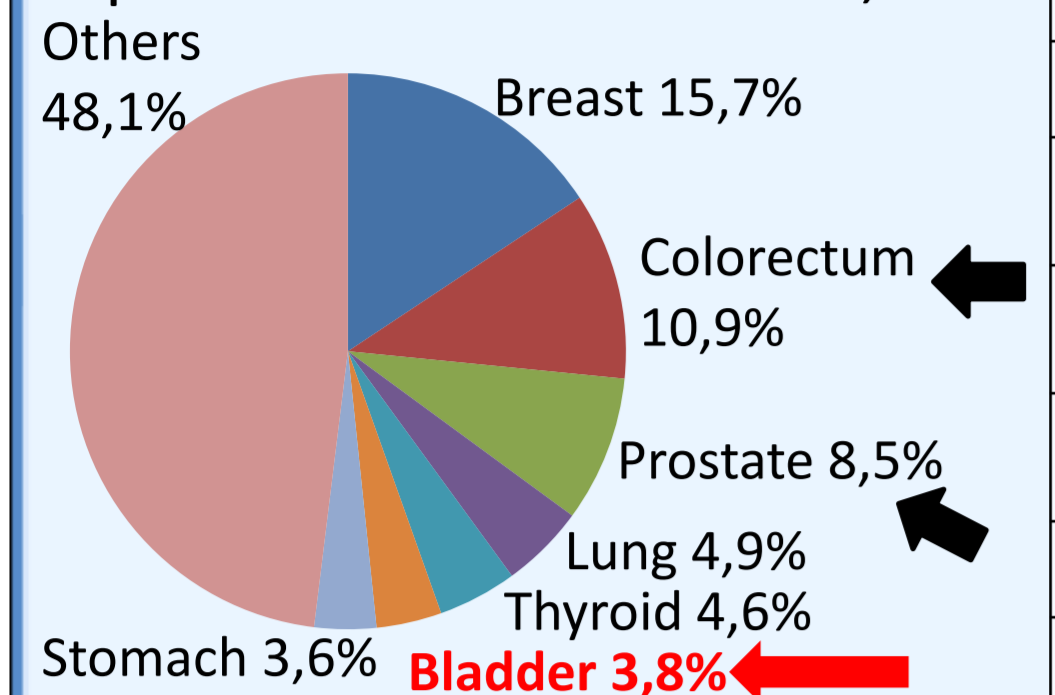
Context: Chronique radiation cystitis (CRC) and treatment

Chronic radiation cystitis = bladder damages due to irradiation of the pelvic area. Involves 5-10% of patients and occur after 6 months¹. The pathology is characterized by a decrease in bladder volume, pain, urgency and hematuria (blood in the urine).

There is no established long term treatment². The consequences are an increasing cost for society (repeated hospitalization for palliative care) and an ethical problem to help these patients with an irreversible degraded quality of life. We propose that cell therapy is a safe and suitable option.

Cancers in the world

Global estimation of the number of prevalent cases of cancer, 2018



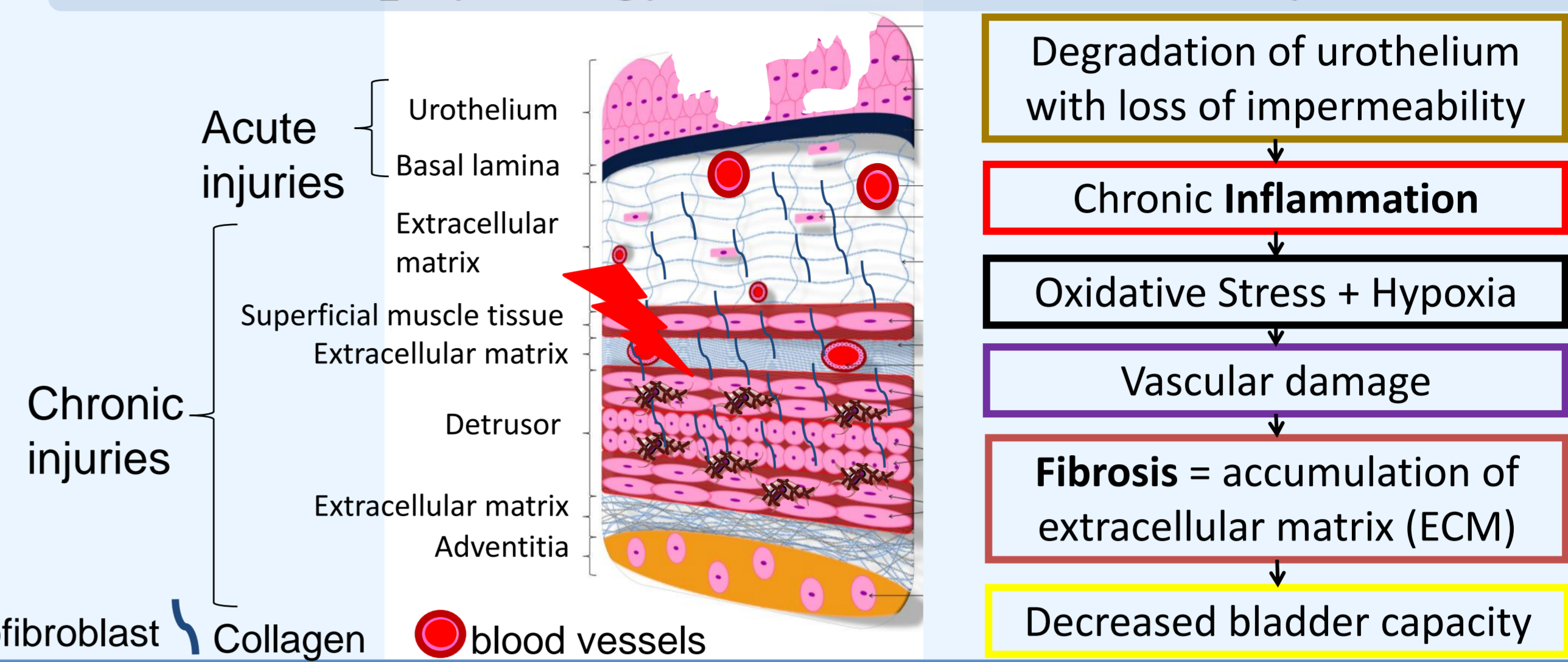
Abdominal-pelvic sphere = 25% of cancers (←⁴).

The bladder is an organ at risk for pelvic radiotherapy.

Organ at risk for pelvic radiotherapy³

| Organs treated by radiotherapy | Risk organs |
|--------------------------------|--|
| Anal duct | Small intestine, bladder , vulva, labia majora |
| Cervix uteri | Rectum, bladder , anal canal, small intestine, sigmoid colon, vagina |
| Endometrium | Rectum, bladder , anal canal, small intestine, sigmoid colon, vagina |
| Vulva | Rectum, bladder , urethra, anal canal, small intestine, sigmoid colon |
| Prostate | Rectum, bladder , anal canal |
| Bladder | Rectum, anal canal, small intestine, sigmoid colon |

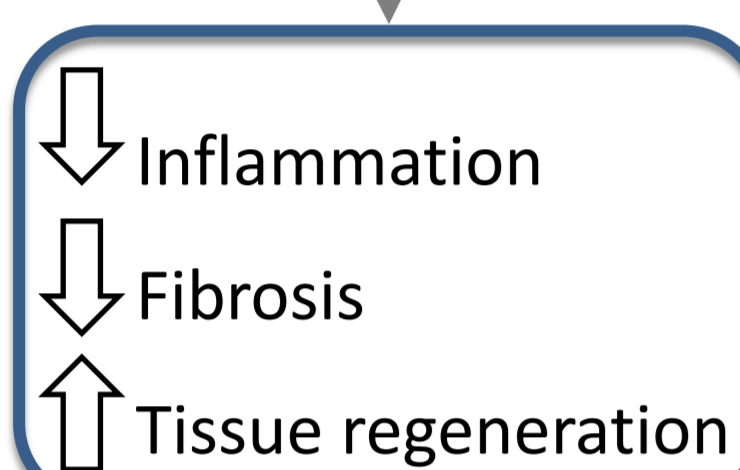
Pathophysiology of chronic radiation cystitis



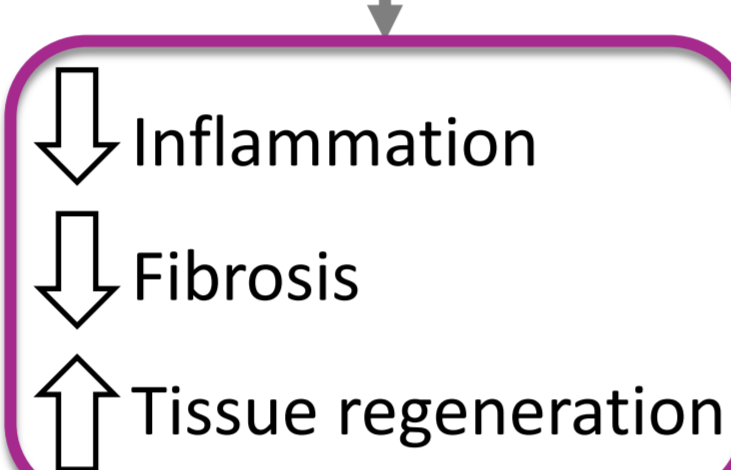
Effects of mesenchymal stem cells in similar CRC pathologies

Mesenchymal Stem Cells (MSC) Effects

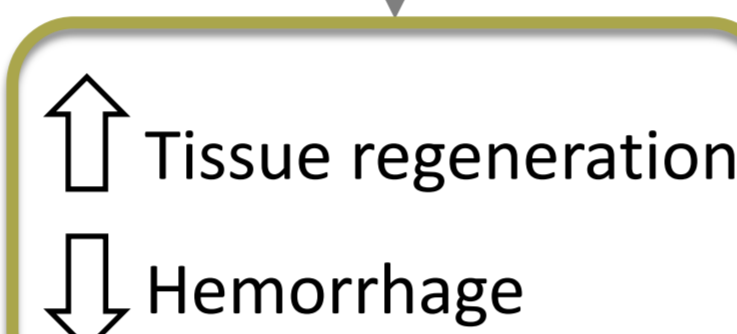
Other pelvic radio-induced diseases
Usunier et al., 2014; Linard et al., 2013



Interstitial cystitis
Kim et al., 2016
Song et al., 2015



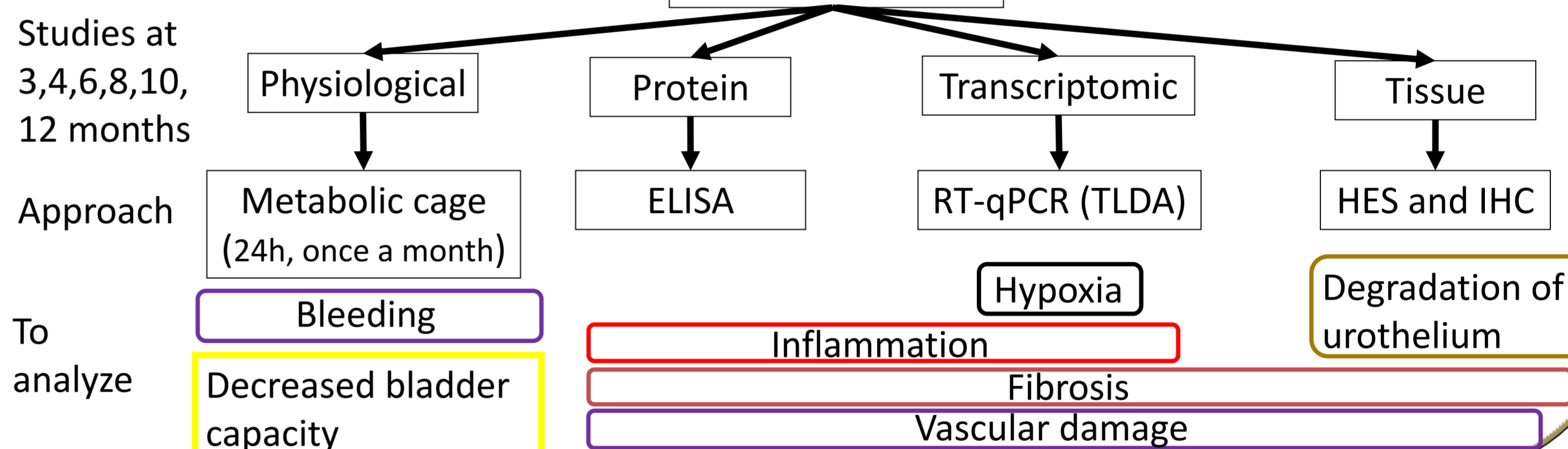
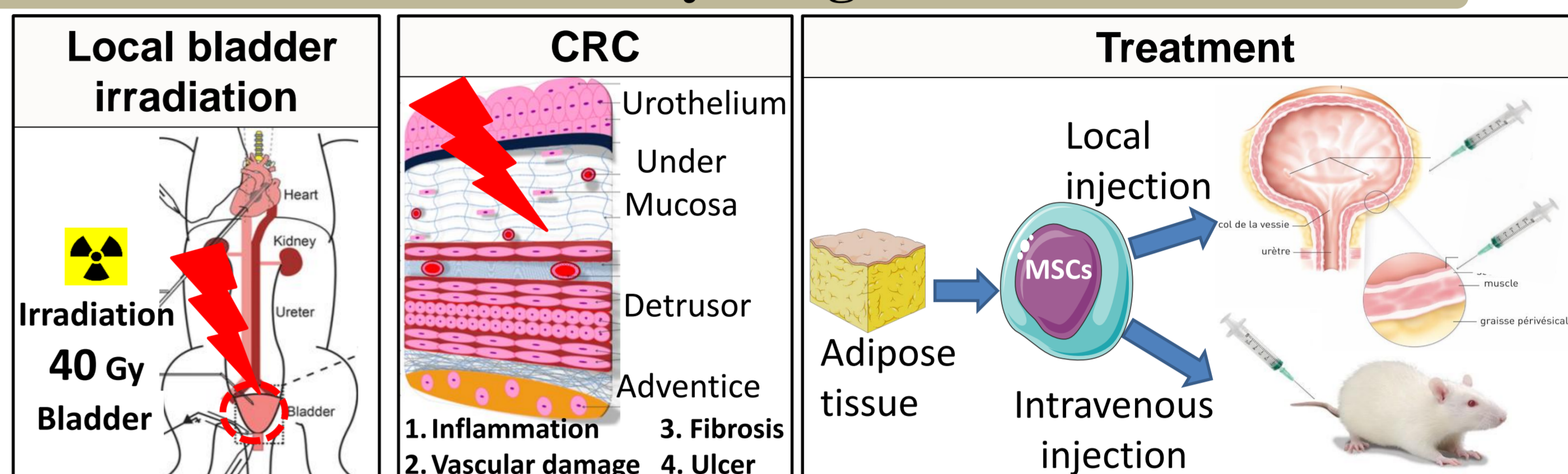
Hemorrhagic cystitis
Lee et al., 2003; Ringden et al. 2007



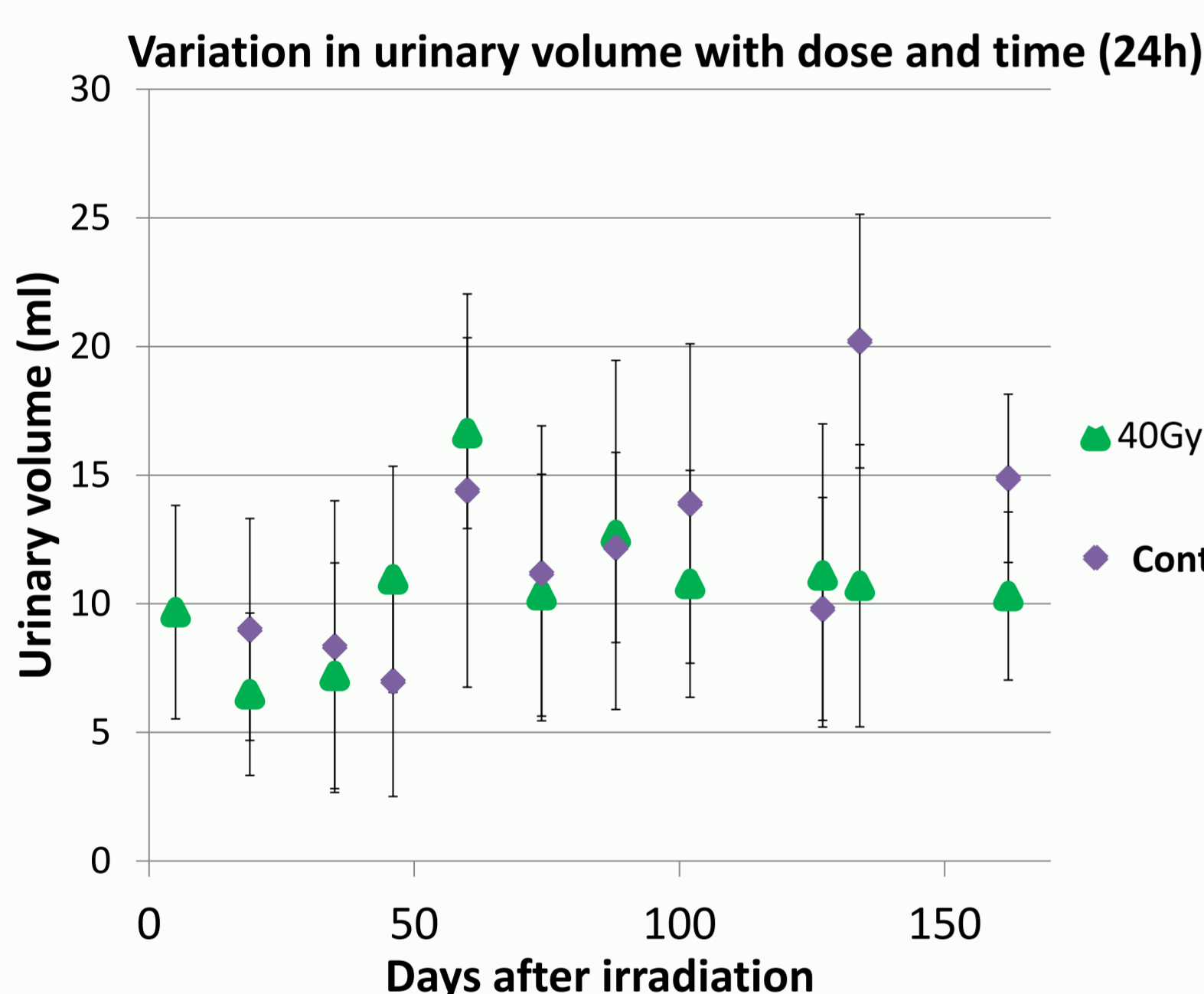
MSCs have a significant effect on diseases similar to CRC. However, this one has not been tested on CRC.

Hypothesis: MSCs could reduce inflammation, fibrosis and could increase tissue regeneration in CRC

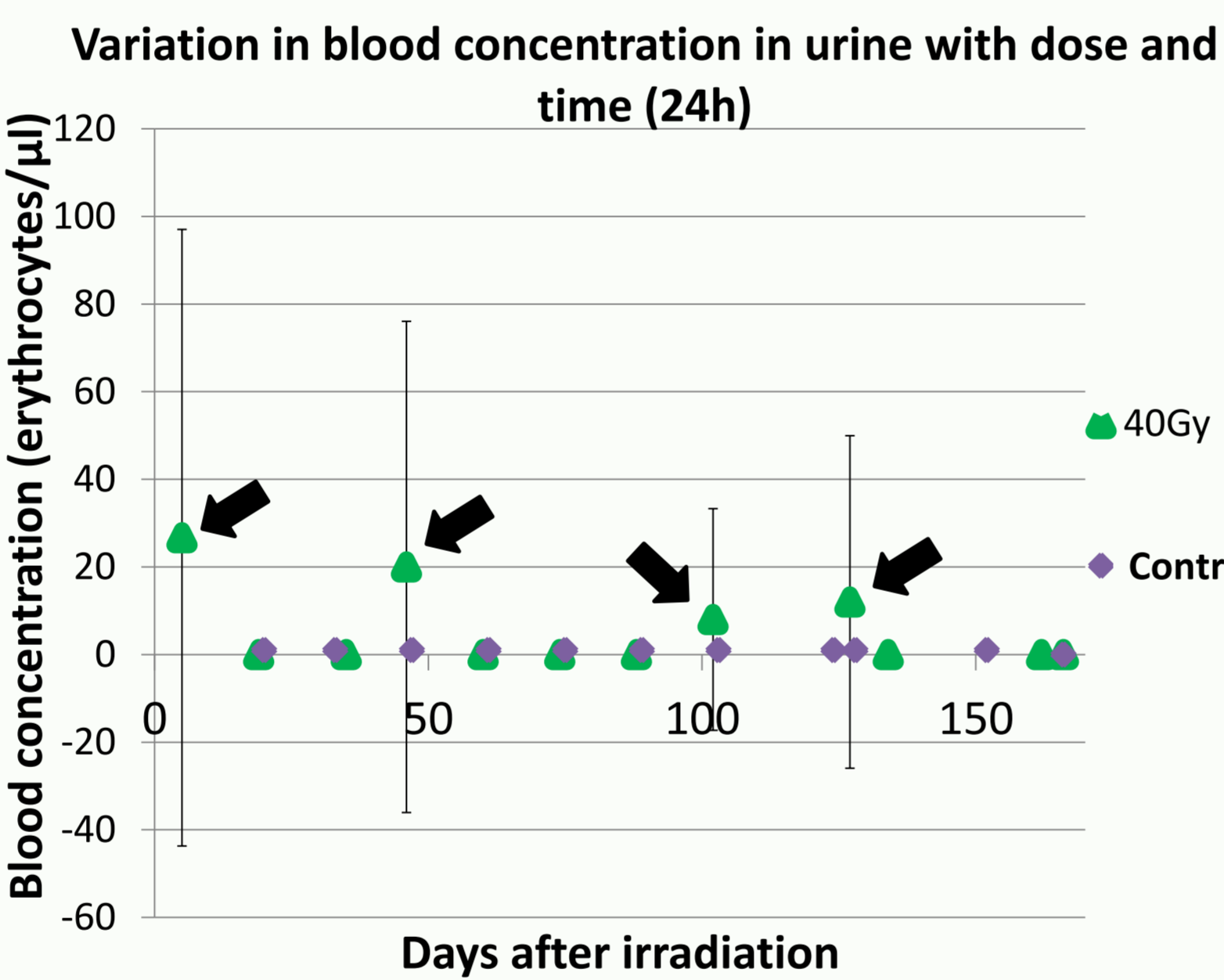
Study design



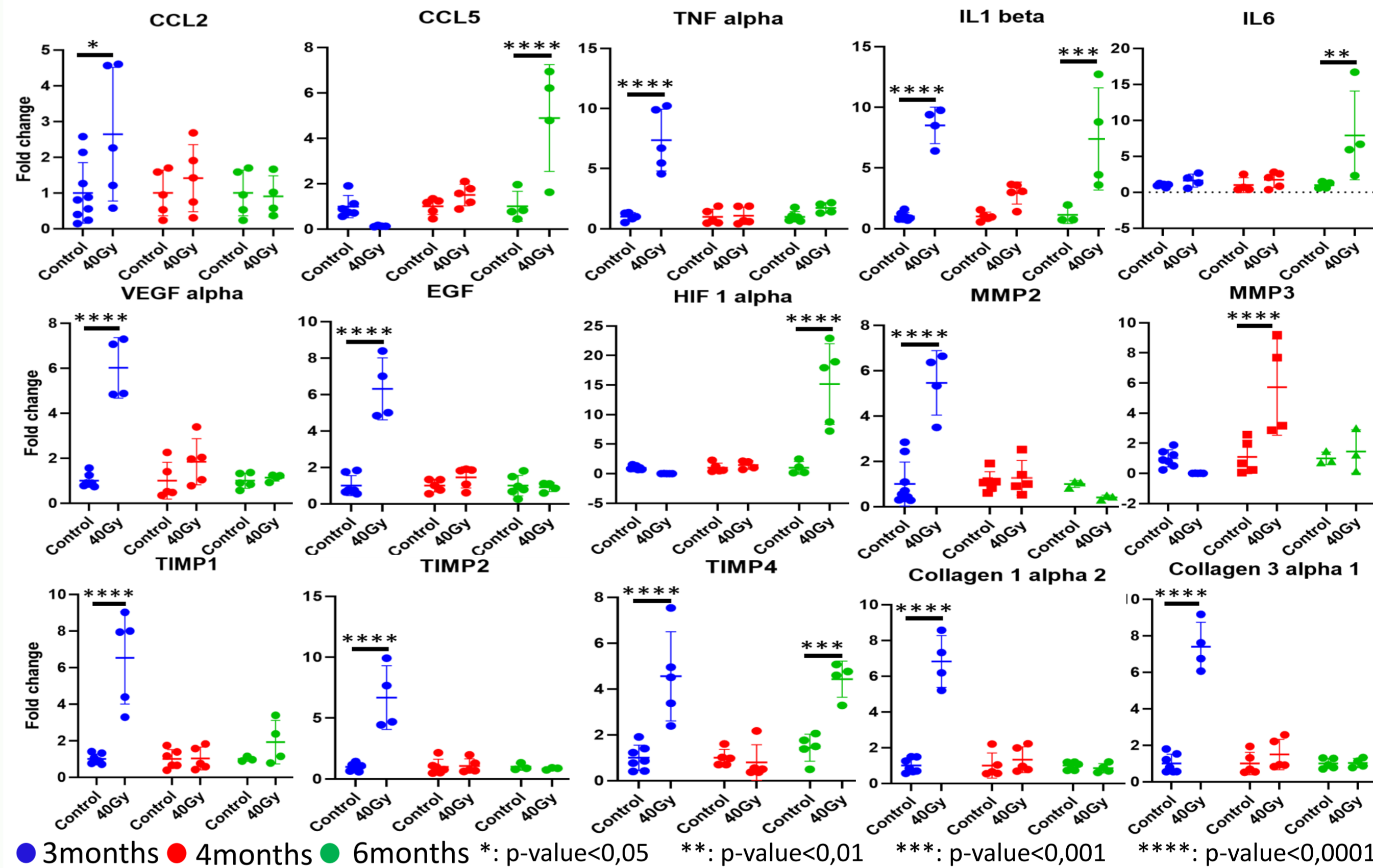
Physiological studies: urinary parameters (volume, hematuria)



No decrease in urine volume during the six months.
Transient hematuria (←) were observed in rats irradiated at 40 Gy.

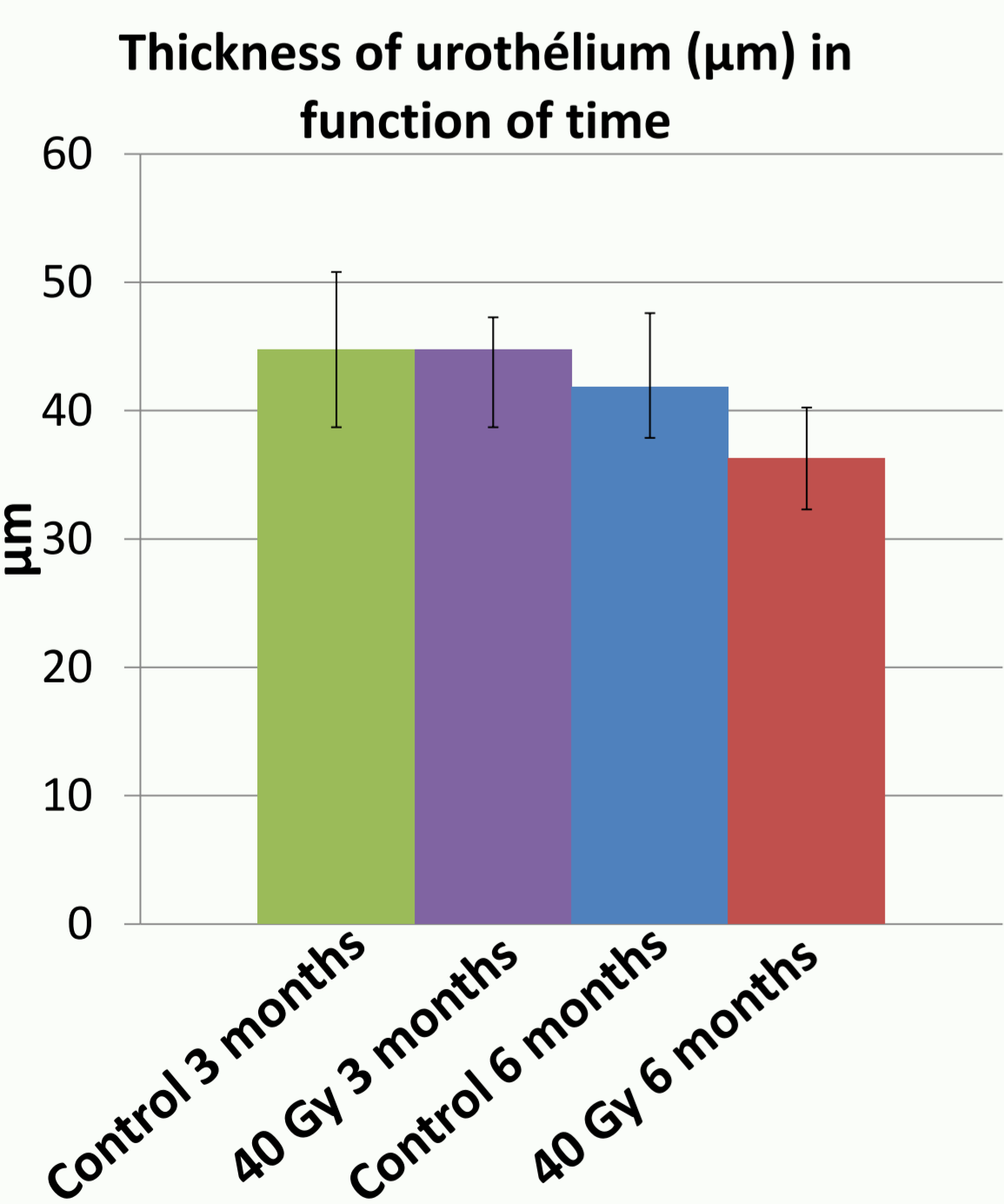


Transcriptomics studies: fibrosis, regeneration and inflammation

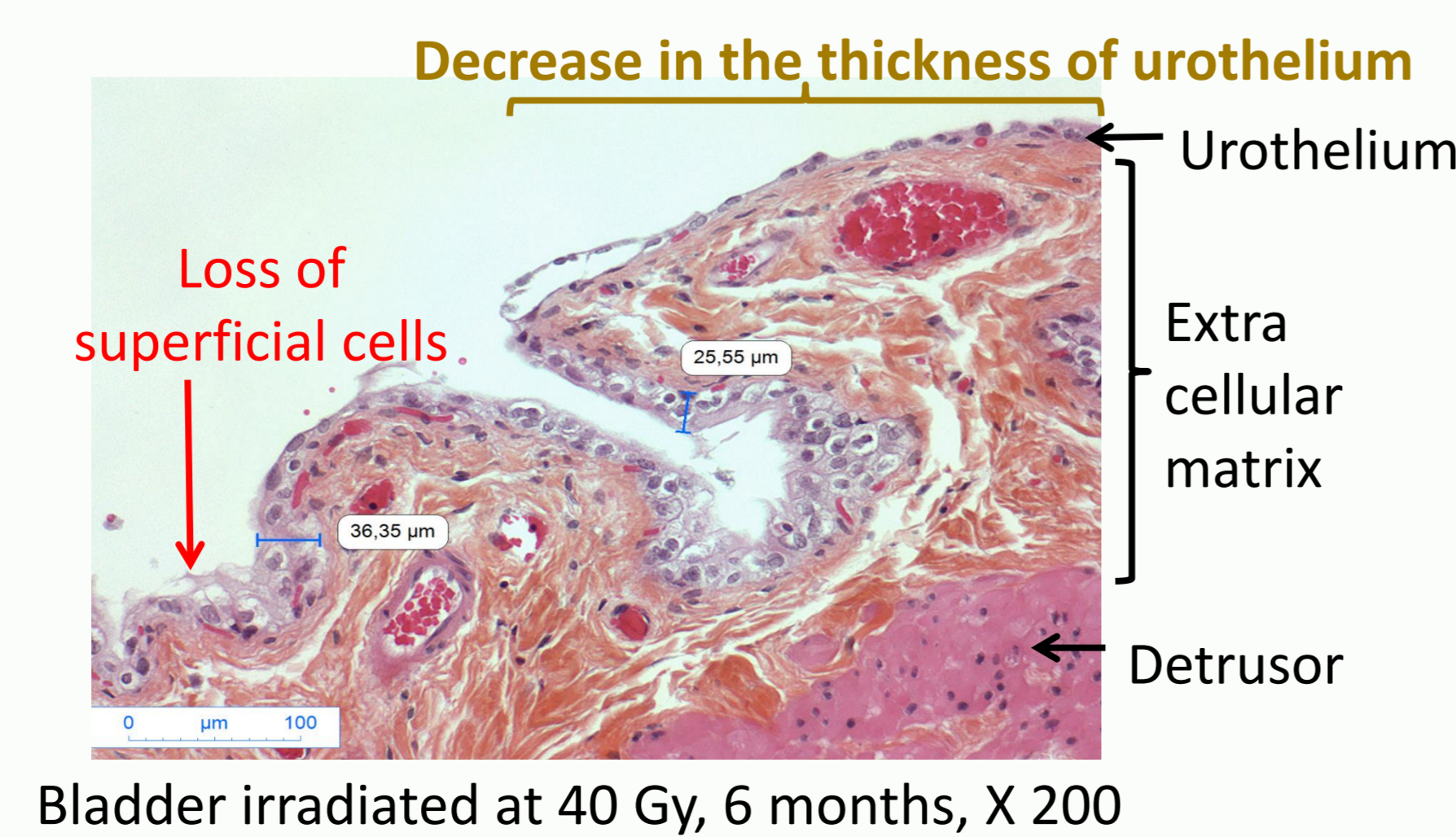
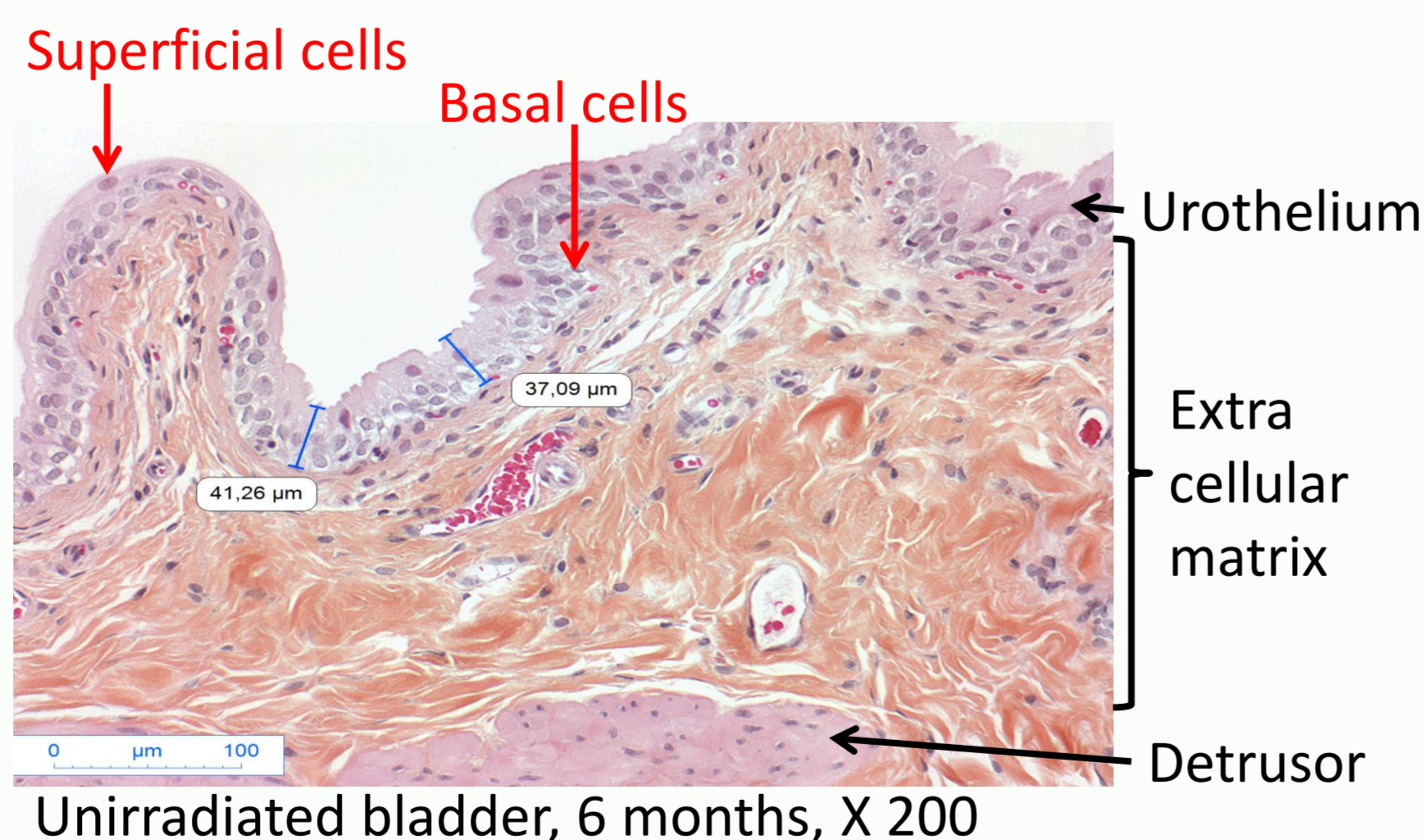


- At 3 months: ↑ Inflammation, tissue regeneration, MEC remodeling.
- At 6 months: ↑ Inflammation, hypoxia.
- These results support an **initiation of chronic phase**.

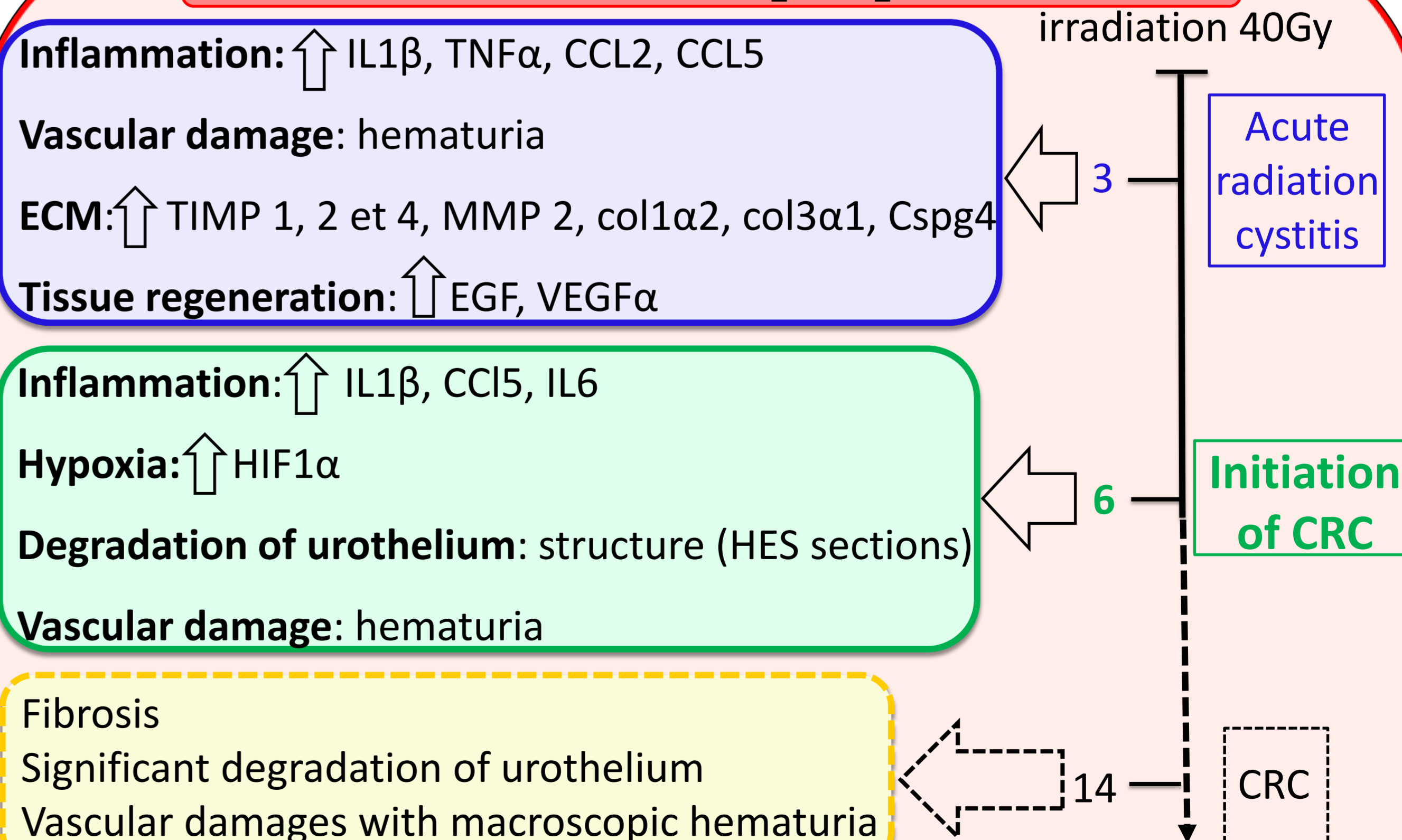
Tissue study: urothelium damages (HES)



- Degradation of the urothelium structure
- Without any significant decrease in urothelium thickness.



Conclusions and perspectives



6 months = Initiation of chronic phase

- Longer kinetic for fibrosis development and decreased bladder capacity
- Study of urothelium structure, endoscopy
- 3D bladder scan to follow volume, vascularization and fibrosis

Bibliography

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