

MODELLO SCHEDA RELAZIONE DOTTORANDI

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(massimo 2000 caratteri totali, spazi inclusi)

Descrivere brevemente la propria ricerca, suddividendola in

Titolo: Investigating the benefit of combined androgen deprivation therapy and radiotherapy in prostate cancer

- Introduzione

In prostate cancer(PCa),a survival benefit is evident when long-term adjuvant androgen deprivation therapy (LTADT) is added to concurrent ADT and external beam radiotherapy(1)(2),but the timing and duration of ADT are still critical(3).

Though hypoxia interferes with the fixation of DNA damage,laying the basis for radioresistance(4),the impact of hypoxia on PCa progression following prostatectomy or radiotherapy is poorly understood.So,the link between radiotherapy,ADT and hypoxia is essential in the comprehension of PCa and further studies are quickly required.

- Metodiche utilizzate

LNCaP and LNCaP R-bic(continuous exposure to20μM R-bicalutamide)cell lines were used.

Up to now,cells are kept in continuous hypoxic conditions(1%O₂) for13weeks.Chronic hypoxia-conditioned cells will be establish at6months of continuous exposure(5).Normoxic samples were run in parallel.

Methods performed:

- 3D culture(pellet culture system,(6))
- Real-Time PCR(AR,PSA,HIF-1α,SLUG,SNAI1)
- WB(e-cadherin,AR,PSA,Fibronectin,Twist,Vinculin)
- Prostasphere formation assay(7)

- Risultati ottenuti At the time of drawing this text,all experiments were performed once or are still ongoing.I've just started the characterization of hypoxic PCa cells lines,to evaluate the differences with their normoxic counterparts.I thought about experiments that could cover different fields of knowledge.Periodic extraction of RNA and proteins let me monitor the developing modifications concerning EMT processes(SNAI, SLUG expression levels by Real-Time PCR;e-cadherin protein by WB).Then,as it's reported that hypoxia switches on a stemness genes signature,I set up the prostasphere formation assay(now I have obtained the primary spherical population).Furthermore,I investigated fluctuations of AR and PSA(one of its crucial target gene)expression in hypoxia.Finally,as in practical routine I noticed that hypoxic cells acquires a stronger adhesive capability,I will investigate the cellular adhesion

mechanisms altered in hypoxia(Vinculin, fibronectin, twist,e-cadherin protein detection by WB).

Bibliografia

1. Horwitz EM, Bae K, Hanks GE, Porter A, Grignon DJ, Brereton HD, et al. Ten-year follow-up of radiation therapy oncology group protocol 92-02: a phase III trial of the duration of elective androgen deprivation in locally advanced prostate cancer. J Clin Oncol. 2008 May 20;26(15):2497-504.
2. Bolla M, de Reijke TM, Van Tienhoven G, Van den Bergh AC, Oddens J, Poortmans PM, et al. Duration of androgen suppression in the treatment of prostate cancer. N Engl J Med. 2009 Jun 11;360(24):2516-27.
3. Pisansky TM, Hunt D, Gomella LG, Amin MB, Balogh AG, Chinn DM, et al. Duration of androgen suppression before radiotherapy for localized prostate cancer: radiation therapy oncology group randomized clinical trial 9910. J Clin Oncol. 2015 Feb 1;33(4):332-9.
4. Hockel M, Vaupel P. Tumor hypoxia: definitions and current clinical, biologic, and molecular aspects. J Natl Cancer Inst. 2001 Feb 21;93(4):266-76.
5. Yamasaki M, Nomura T, Sato F, Mimata H. Chronic hypoxia induces androgen-independent and invasive behavior in LNCaP human prostate cancer cells. Urol Oncol 2013(31): 1124-31.
6. Zanoni, M. et al. 3D tumor spheroid models for in vitro therapeutic screening: a systematic approach to enhance the biological relevance of data obtained. Sci. Rep. 6, 19103.
7. Bisson I, Prowse DM. WNT signaling regulates self-renewal and differentiation of prostate cancer cells with stem cell characteristics. Cell Research (2009) 19:683-697.

• Abstracts e partecipazione a congressi e corsi: autori, titolo della presentazione, nome e date del congresso

• Pubblicazioni scientifiche: autori, titolo della pubblicazione, nome e numero della rivista, anno di pubblicazione

1. Zanoni, M, Piccinini F, Arienti C, **Zamagni A**, Santi S, Polico R, Bevilacqua A, Tesei A. 3D tumor spheroid models for in vitro therapeutic screening: a systematic approach to enhance the biological relevance of data obtained. Sci. Rep. 6, 19103
2. Rui M, Rossi D, Marra A, Paolillo M, Schinelli S, Curti D, Tesei A, Cortesi M, **Zamagni A**, Laurini E, Pricl S, Schepmann D, Wünsch B, Urban E, Pace V, Collina S. Synthesis and biological evaluation of new aryl-alkyl(alkenyl)-4-benzylpiperidines, novel Sigma Receptor (SR) modulators, as potential anticancer-agents. Eur J Med Chem. 2016 Aug 31;124:649-665

• Eventuali soggiorni in altri laboratori italiani o esteri

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