***Relazioni attività di ricerca* – II anno XXXV ciclo:**

Manuela Montanaro, XXXV ciclo
Docente guida: Prof. Alessandro Mauriello

Identification of New Biomarkers of Mineralization and Vulnerability in Carotid Atheromatous Plaques

Atherosclerosis is a chronic and progressive vascular disease with a multifactorial aetiology in which modifiable and non-modifiable risk factors may play crucial roles in pathology progression. Ectopic calcifications in carotid plaque may also contribute to its vulnerability. Starting from these considerations, this project aims to analyse some of the mechanisms involved in both carotid plaque instability and atheromatous calcifications. Our previous studies reported a different calcium salts composition in calcifications, depending on plaque stability and/or on the presence of heavy metals contaminants (i.e. aluminium). Also, the main inflammatory and mineralization markers have been investigated, revealing an increase of IL6 and IL17 expression in unstable plaques of female patients, as well as an association between BMP-2 and Calmodulin with plaque instability. As concern the inflammatory biomarkers, also the C-Reactive Protein (CRP) levels have been assessed. Specifically, high CRP increase the carotid instability risk in dyslipidemic males. Regarding the presence of heavy metals, questionnaires about lifestyle have been administered. Interestingly, ultrastructure analysis demonstrated the presence of aluminium in 5 patients with an history of contaminated exposure, including environment or specific therapies. These data lay the foundations for further studies focused on the effects of contaminants in carotid plaque evolution.

Rosalba Pecorari, XXXV ciclo
Docente guida: Prof.ssa Eleonora Candi

Defining the p63 interactome in squamous cell carcinoma tumors

The transcription factor TP63 is known for its role in the regulation of epithelial morphogenesis and adult stem cells maintenance. It has also a role in tumorigenesis and cancer progression. In fact, is it amplified in head and neck squamous cell carcinomas (HNSCC), in which ΔNp63α (referred in here as p63) is the main overexpressed isoform, with oncogenic function. To unveil its oncogenic role in HNSCC we focused on the p63 interactome. We first underlined the p63 putative interactome through a BioID (Proximity-dependent Biotin Identification) assay. We decided to study the interaction between p63 and ZNF148. ZNF148, is a Krüppel-type zinc-finger transcription factor and acts as a transcriptional activator or repressor of several genes. By Co-immunoprecipitation, we first confirmed p63 and ZNF148 direct interaction. ChIPseq experiments for p63 and ZNF148 showed that the two factors share several binding sites on DNA (2688 co-regulated genes). Among these genes, several are associated to cell cycle and cancer maintenance and progression pathways, in which the most represented one is CCND1. As matter of fact, ZNF148 and p63-silencing lead to proliferation rate reduction, indicating that both p63 and ZNF148 cooperated to regulate cell cycle progression, in part by controlling the CCND1 expression. Further studies will be done to confirm this link in vivo (tumour xenograft experiments) and in patient tissues (tissue microarray of HNSCCs or analysis of patient biopsies). To further elucidate the role of p63 and ZNF148 interaction we performed a RNAseq experiment after the silencing of both proteins. Go term analysis revealed that mainly ZNF148, and partially p63, regulates the expression of keys genes involved in Interferons signaling. This aspect needs to be further validated and investigated. The data obtained so far, suggested that in HNSCC cell lines, p63 and ZNF148 act synergistically to promote proliferation.

Adelaide Teofani, XXXV ciclo
Docente guida: Prof. Alessandro Desideri

Intestinal taxa abundance and diversity in inflammatory bowel disease patients: an analysis including covariates and confounders

Inflammatory bowel diseases (IBD), which include Crohn's disease (CD) and ulcerative colitis (UC), are chronic immune-mediated disorders of the gastrointestinal tract of unknown aetiology. Many evidences suggest that the pathological status is the result of an interaction between genetic and environmental factors, leading to an abnormal immune response against the human microbiome. In order to investigate the impact of lifestyle and dietary habits on the modulation of intestinal taxa abundance and diversity in inflammatory bowel diseases, a 16S rRNA gene analysis was performed using genomic DNA extracted from faecal samples of 52 patients with Crohn's disease (CD), 58 patients with ulcerative colitis (UC) and 42 healthy controls (HC). Results indicated a reduced microbial diversity in CD and UC patients compared to HC. Some of the variables related to patient's age, lifestyle and dietary habits resulted to be significantly unbalanced across the CD, UC and HC groups, acting as confounders and thus influencing alterations in the abundance of specific microbial families. The abundance of *Atopobiaceae* and *Defluvitaleacae* bacterial families appears in fact to be differentially modulated when including in the analysis the confounders and the covariates. In detail, the results indicate an association between the *Atopobiaceae* family and the cereals consumption, as also supported by the literature. In conclusion, correcting the analysis by covariates and confounders permits to identify the bacterial families whose abundance is only modulated by the IBD status.

Emanuele Criscuolo, XXXV ciclo
Docente guida: Dr.ssa Filomena Fezza

Protein activity investigations using multidisciplinary approaches

The endocannabinoid system (ECS) is an evolutionarily conserved lipid signalling system, which comprises endocannabinoids, their principal target receptors, the cannabinoid 1 (CB1R) and 2 (CB2R) receptor and their metabolic enzymes, such as Fatty Acid Amide Hydrolase (FAAH). To study the potential interaction between CB1R and active substances I used computational analysis (virtual screening) using a database of FDA drugs (composed by about 4200 compounds). After the virtual screening, I have selected about 40 molecules that were processed with another computational procedure to ascertain their selectivity on CB1R and so, I obtained the top 10 molecules. At the same time, I built human FAAH model, using in silico technique, in order to compare rat and human structures and their behaviour with the major phytocannabinoids. I've performed enzymatic activity assay as well, to verify the potency of each compounds using rat FAAH and human FAAH. Finally, we matched in vitro and in silico results to better understand the mechanism of this enzyme and the interspecies differences. Lastly, I studied New Delhi metallo-beta-lactamase (NDM-1), an enzyme that makes bacteria resistant to a broad range of beta-lactam. Molecular dynamics simulations were performed to justify the differences observed in the kinetic behaviour of some NDM-1 mutants.

Raffaele Dante Caposiena Caro, XXXV ciclo
Capo dipartimento/laboratorio: Prof.ssa Iris Zalaudek
Docente guida: Prof. Luca Bianchi

Factors related to the onset and recurrence of flares in hidradenitis suppurativa patients treated with adalimumab

Hidradenitis suppurativa (HS) is characterized by periodic worsening of symptoms. The aim was to investigate factors associated with flare outbreak in HS patients in treatment with adalimumab. In total, 115 HS patients treated with adalimumab from 5 Italian centers were reviewed. Clinical and epidemiological data were collected at baseline. Flares were modelled with baseline features using univariate and multivariate Cox-regression. The factors significantly correlated with flares in the univariate model were analyzed using a recurrent event survival analysis (Andersen-Gill model) to assess the relation between them and flares recurrence. During the observation period 80.9% of patients developed flares, detecting 252 flares, overall. A univariate model identified five risk factors associated with the outbreak of flares. While, the Andersen-Gill model showed four factors correlated with flares recurrence. An early treatment of HS may prevent both the disease progression and reduce the recurrence of flares.

Lucas Fabrício Bahia Nogueira, XXXV ciclo
Docente guida: Prof. Massimo Bottini
tutor: Prof. Ana Paula Ramos (University of São Paulo, Brazil)

Collagen/κ-carrageenan based scaffolds as biomimetic bone tissue constructs: a model system for in vitro bone mineralization studies.

In this study, we used collagen in the production of 3D mineralized biomimetic matrices mimicking the microenvironment of native bone. κ-carrageenan (κ-Carr) was added to the scaffolds in an attempt to fulfill the role of sulfated glycosaminoglycan in the bone matrix, because κ-Carr has the advantage of extracting it from renewable sources (i.e., red algae). Ordered matrices were obtained by exploring the property of type I collagen molecules to self-assemble in highly aligned fibrils by the increase in pH and slow evaporation of solutions at high concentration. Scanning electron microscopy imaging showed the presence of uniform fibrils compacted and intertwined in a dense network. Side views of the samples showed collagen fibrils with a parallel alignment, which is characteristic in dense connective tissues. The incorporation of κ-Carr resulted in a significant change in the surface morphology to a highly rugged irregular and non-periodic pattern. The scaffolds obtained before and after the incorporation of κ-Carr supported osteoblasts proliferation. Our results showed that reproducing the fibrillar structure by the chemical method of pH control is a suitable alternative to design an appropriate model to study the role of structural organization of artificial extracellular matrix in cell behavior.

***Relazione attività di ricerca* - I anno XXXVI ciclo:**

Carlotta Zampieri, XXXVI ciclo
Docente guida: Ivano Amelio

p53 mutation defines chromatin state to confer drug tolerant phenotype in cancer

Somatic inactivation of p53 in cancer frequently occurs as missense mutations that lead to acquisition of neomorphic mutant protein forms. p53 mutants have been postulated to exert gain-of-function (GOF) effects, including promotion of metastasis and drug tolerance, which generally contribute to acquisition of the lethal phenotype. In this study, by integrating a p53R270H-dependent transcriptomic analysis with chromatin accessibility (ATAC-seq) profiling, we shed light on the molecular basis of p53 mutant-dependent drug tolerant phenotype in pancreatic cancer. p53R270H finely tunes chromatin state in specific genomic loci orchestrating a transcriptional programme that participates to phenotypic evolution of the cancer. We specifically focused on the p53R270H-dependent regulation of the tyrosine kinase receptor MST1r. MST1r deregulation substantially impinged on drug response in experimental model, recapitulating the p53R270H-dependent phenotype, and strongly correlated with p53 mutant and aggressive phenotype in pancreatic cancer patients. As cellular plasticity in staged pancreatic cancer seems to predominantly originate from epigenetic mechanisms, we propose that mutant p53 participates in acquisition of lethal phenotype by finely tuning chromatin state.

Silvia Buonvino, XXXVI ciclo
Docente guida: Prof. Sonia Melino

H_2S donors for Optimization of 3D Culture Systems for Stem Cell Therapy in Tissue Regeneration

Photopolymerized hydrogels are ideal materials to improve stem cell-based tissue regeneration but our experiments brought to light that photopolymerization may itself cause cell damage requiring conjugation between proteins and synthetic polymers, photoinitiators and UV exposure for radical monomers crosslink, all processes whose effects on cells are not yet clarified. The gasotransmitter H_2S protects cells from oxidative damage acting as scavenger molecule and inducing the expression of antioxidant proteins. The ability of a glutathione-conjugated garlic extract (GSGa), that slowly releases H_2S and produced in our laboratory, to prevent photopolymerization (PhP) damage was evaluated using both an enzymatic model and a cardiac mesenchymal stem cells (cMSCs) 3D culture based on PEG fibrinogen hydrogel (PFHy). The decreased activity of a recombinant cyanide:thiosulfate sulfurtransferase (TST,EC. 2.8.1.1) exposed to PEGDa and UV light was inhibited by the presence of GSGa. Western blot analysis showed that in cMSCs GSGa induced the upregulation of Antioxidant Responsive Elements (ARE) controlled enzymes expression. We also proved that the preconditioning of cMSCs with GSGa before embedding into PFHy exerts protective effects from PhP damage. These findings pave the way for the use of H_2S donors in cells pretreatment for tissue engineering applications, such as tissue repairing and 3D bioprinting.

Valentina Tullio, XXXVI ciclo
Docente guida: Dott. Valeria Gasperi

MiR 126 in breast cancer and platelets

We have previously shown that miR-126 plays a suppressor role in human breast cancer (BC) cells by directly targeting AKT2, a kinase involved in invasion and metastasis pathways. We deepen our investigation by analyzing the *in vitro* and *in vivo* role of miR-126 and its target AKT2 in BC.

We firstly investigated whether miR-126, by targeting AKT2, might impact *in vitro* proliferative (analyzed by CFU assay) and invasive (analyzed by Matrigel Transwell Invasion Assay) properties of different BC cell lines. We found that both the invasiveness and proliferative capacity of BC cells are related to levels of miR-126 and AKT2, and this kinase, known as exclusively involved in steps of the metastatic process of BC, also promotes the first steps of oncogenesis. miR126 overexpression, as well as AKT2 silencing, indeed, significantly decreased the number of colonies, as well as that of invading cells. We also set up a fast and reproducible quantitative method for CFU assay, based on elution of bound crystal violet, that gave results superimposable to those obtained with the common method of colony counting. To corroborate *in vitro* results, we performed bioinformatic studies, finding that overall survival (OS) of patients with different BC subtypes is directly correlated with miR-126 expression, while being inversely correlated with AKT2 expression. Collectively, our data strongly suggest that miR-126 and AKT2 expression might have a prognostic value in BC.

Erica Foffi, XXXVI ciclo
Tutor: Prof. Eleonora Candi

Identification of positive transcriptional effectors of ΔNp63 in epithelia

ΔNp63 is a transcription factor known for its role in the regulation of epithelial morphogenesis and adult epithelial stem cell maintenance and differentiation. It also plays a role in tumorigenesis: it is upregulated in 20% of the head and neck squamous cell carcinomas (HNSCC), having an oncogenic function. Preliminary data obtained by a BioID (Proximity-dependent Biotin Identification) assay, underlined the ΔNp63 putative interactome. We decided to study the interaction between ΔNp63 and the chromatin reader Bromodomain-containing protein 4 (BRD4). BRD4 recognizes and binds acetylated histones and mediates the expression of a wide range of genes. Recent findings indicate BRD4 as a novel cancer therapeutic target. Our data indicate that, in human keratinocytes, p63 and BRD4 interaction is required for p63-mediated transcriptional programs, including proliferation, cellular metabolism, and differentiation. p63 and BRD4 expression are positive correlated in normal squamous epithelia, in addition a positive correlation is also observed in HNSCC patient datasets. We aim in future experiments to extend our analyses in HNSCC cancer cell lines, to understand if BRD4 can be also a positive effector of ΔNp63 to mediate its oncogenic activity.

Eleonora Mammarella, XXXVI ciclo
Docente guida: Ivano Amelio

Epigenetic regulation of p53 in tumor suppression

Tumor suppressor protein 53 (TP53), is among the crucial players of tumour suppression and maintenance of the genome integrity. Missense mutations in this gene lead to the acquisition of new oncogenic functions, collectively referred to as gain of function (GOF) effects. In the first part of my PhD project, I studied the gene regulatory network of p53 mutant, while part of my activity was directed to the calibration of a system for epigenetic analysis by live cell imaging. To help dissecting the molecular basis of p53 mutant GOF, we conducted an analysis of a fully annotated genomic and transcriptomic human pancreatic adenocarcinoma dataset. Genes of interest were selected on the basis of their differential expression between p53 mutant and p53 wild-type cohorts and their prognostic value. We identified NUAK2 and RCAN2 as candidate players of p53 mutant network. We validated their regulation in cellular models and analysed Chip-Seq data to identify hypothetical molecular mechanism through p53 mutant could modulate their expression. We found that p53 can physically bind RCAN2 gene locus in the regulatory regions where is known binding of the other p53 mutant interactors as Srebp1 and p63, indicating the existence of this molecular mechanism. In the second part of PhD project, I calibrated a system to perform Live Cell Imaging and detect specific epigenetic

modification in living cells. I used engineered proteins with DNA binding domain able to recognize and mark specific epigenetic target as DNA methylation and histone 3 lysine 9 trimethylation in mouse Major Satellite, pericentromeric regions of DNA repeats in tandem. This system is composed by two modules, respectively the first one specific to recognize the epigenetic modification of interest and the second one, able to mark Major Satellite repeats. Both modules were combined to two domains of the Venus fluorophores capable of emitting a fluorescent signal that can be microscopically tracked. The probes were tested on different cellular systems p53 wild type and null, then, in future studies, I will deepen the role of p53 on the stability of the pericentromeric regions in cellular model of Pancreatic Adenocarcinoma.

Francesco Moro, XXXVI ciclo
Tutor: Dott. Giovanni Di Zenzo
Docente guida: Prof. Eleonora Candi

A case-control study on the association of dipeptidyl peptidase IV inhibitor (gliptin) treatment in type 2 diabetes and bullous pemphigoid

Bullous pemphigoid (BP) is the most frequent autoimmune blistering disease and is induced by autoantibodies against two structural proteins of the dermal-epidermal junction, i.e. BP180 and BP230. The vast majority of the autoAbs target the extracellular noncollagenous 16A domain (NC16A) of BP180. Moreover, BP- autoAbs may target epitopes other than the NC16A domain. Correlations between targeted epitopes and clinical features have not been fully investigated. Recently, several cases of BP have been reported in patients treated with dipeptidyl peptidase-IV inhibitors (DPP4i), also termed gliptins (GPs), for type-2 diabetes (T2D). To estimate the extent of association between GP treatment and BP onset, and to determine whether specific GPs have different roles we are conducting a case-control study with prospective enrollment on cases' raw. Thus, cases are represented by patients with BP and diabetes, the control series is formed by patients without BP and with T2D. We are evaluating clinical features, disease severity, time to disease activity control, and complete remission in 12 months follow-up period. We are assessing the relevance of different classes of Immunoglobulin (IgG, IgE, and IgA) in the humoral autoimmune response against BP antigens in different subsets of BP patients and controls. In addition, the immune response will be epitope mapped using different BP180 portions.

XXXIV

Francesco Rugolo, PhD Student, XXXIV ciclo
Tutor: Prof. Massimiliano Agostini

The expression of ELOVL4, repressed by MYCN, defines neuroblastoma patients with good outcome. During my PhD, my main project focused on the study of the enzyme ELOLV4, both from the point of view of its transcriptional regulation and its role in neuroblastoma cells. ELOVL4 is an enzyme belonging to the class of elongase of fatty acids, involved in the synthesis of VLC-FA and VLC-PUFA and elovanoids, polyunsaturated and oxygenated fatty acids with 32 and 34 carbon atoms and furthermore, its expression is essential for the growth and development of the organism. By consulting different bioinformatics software, we initially identified specific E-box sequences on the ELOVL4 promoter for MYCN, the main transcription factor known in neuroblastoma cells and an important tumour marker as it is always associated with a poor prognosis in patients. Chromatin immunoprecipitation experiments confirmed the presence of MYCN on the ELOVL4 promoter. Further analysis revealed the presence of other important chromatin remodelers (Sp1, HDAC1/2) on the ELOVL4 promoter. Subsequently, through gene silencing experiments or MYCN over-expression

experiments, we simultaneously observed an opposite trend in ELOVL4 expression compare with MYCN expression. For what concern about the biological role of ELOVL4, using fluorescence microscopy, we observed the involvement of ELOVL4 in the production of intracellular Lipid Droplets (LDs); also, we observed that a decrease in ELOVL4 expression is associated with a reduction in neurite outgrowth in neuroblastoma cells. Consistent with this finding, using public datasets of neuroblastoma patients, we observed that ELOVL4 expression is associated with a favourable prognosis. All these data led us to the conclusion that not only ELOVL4 might be negatively regulated in its expression by MYCN in possible association with HDAC1/2 and Sp1, but that it might also act as a prognostic marker in neuroblastoma patients in the future.

Pubblications

1) **Francesco Rugolo**, Nicolas G Bazan, Jorgelina Calandria, Bokkyoo Jun, Giuseppe Raschellà, Gerry Melino, Massimiliano Agostini. (2021). The expression of ELOVL4, repressed by MYCN, defines neuroblastoma patients with good outcome. *Oncogene*. 2021 Jul 31. doi:10.1038/s41388-021-01959-3.
2) Alessio Butera, Matteo Cassandri, **Francesco Rugolo**, Massimiliano Agostini, Gerry Melino. (2020). The ZNF750-RAC1 axis as potential prognostic factor for breast cancer. *Cell Death and Discovery*. 2020 Nov 29;6(1):135.

Cristina Mimma Ruggiero
Tutor: Prof.ssa Alessandra Gambacurta

Epigenetics is considered a new tool for early diagnosis in the representation of the presence of tumor phenotypes. To date, research is focused on the study of DNA methylation, but a new path is opening up towards epigenetic modifications related to histones. They can be useful in discriminating between normal tumor or tissue. Starting from the in vitro analysis on neuroblastoma we studied the epigenetic changes during its osteogenic differentiation. This wide genomic analysis allowed us to identify critical changes in some histone H3 lysines. These data were validated in vivo on human biopsies of basalioma, bladder and head-neck cancer and their respective normal parts, by Immunofluorescence analysis, allowing us to assign two different phenotypes (tumor: H3K27me3 +, H3K79me3-, H3K9me2-; normal: H3K27me3 +/-, H3K79me3 +, H3K9me2 +). It was subsequently verified whether these epigenetic changes corresponded to changes in the 3D genome structure between healthy and cancer patients. Using Hi-C data (*High Chromosome Conformation Capture*) from healthy and tumor tissues of patients, the contact matrices of the genome were constructed, and their analysis showed that during passage from a healthy cell to a tumor, drastic structural changes in chromatin occur. To understand if these relevant epigenetic and structural changes corresponded to a transcriptional dysregulation, the most up and down regulated genes in bladder cancer were examined and going to identify with RNA-Seq the specific dysregulation of cancer subtypes. Most of them are not only transcriptionally dysregulated also in other tumors examined by the Gepia 2 Database but fall into highly structurally modified genome regions as confirmed by DNA-methylation experiments related to other solid tumors. An analysis on Gene Ontology places these genes in three very specific categories based on molecular functions. The study of these genes will be useful not only for the identification of new therapeutic targets for personalized medicine and for a possible repositioning of drugs already used for other pathologies, but also for the identification of new diagnostic and prognostic markers.

PUBBLICATIONS

-Monica Bari, Natalia Battista, Giulia Merlini, Marina Fava, **Cristina Ruggiero**, Sara Piccirillo, Giovanni Valentini, Gabriele Mascetti, Alessandra Gambacurta and Mauro Maccarrone. (2019) “The SERiSM project: preliminary data on human stem cell reprogramming in microgravity” Front. Physiol. Doi: 10.3389/conf.fphys.2018.26.00038

-Alessandra Gambacurta, Giulia Merlini, **Cristina Ruggiero**, Giacomo Diedenhofen, Natalia Battista, Monica Bari, Michele Balsamo, Sara Piccirillo, Giovanni Valentini, Gabriele Mascetti & Mauro Maccarrone-(2019) "Human osteogenic differentiation in Space: proteomic and epigenetic clues to better understand osteoporosis" 9:8343 | https://doi.org/10.1038/s41598-019-44593-6

CONGRESS

-Congress ESA-ESTEC 18-22 JUNE The Netherlands by abstract: The SERISM project: "Modulation of Osteogenic Markers in human Blood-Derived Stem Cells Aboard the ISS during the VITA Mission of the Italian Space Agency"

-Congress «Global Meet on Stem Cell Research and Molecular Biology» 14-OCTOBER 2019 ROME by poster «Human osteogenic differentiation in Space: proteomic and epigenetic clues to better understand osteoporosis».

Carlo Ganini
Tutor: Gennaro Melino

Establishment of a multi-omics approach to cancer

Cancer genomes have been explored from early 2000s through massive exome sequencing, leading to the publication of The Cancer Genome Atlas in 2013. Sequencing techniques have been developed alongside and allowed to go beyond the limitation of costs for whole genome sequencing of single specimens, allowing to develop more accurate and extensive cancer sequencing projects with deep sequencing of whole genomes as well as transcriptomic analysis. The Pan Cancer Analysis of Whole Genomes recently published whole genome sequences data from more than 2600 human cancers together with almost 1200 related transcriptomes. The vast amount of data generated needs to be thoroughly deciphered and the advent of machine learning approaches will be the next step towards the generation of personalized approaches for cancer medicine. Under this light, the generation of other omics data on cancer tissues are still missing, with few databases focusing on proteomics or phospho-proteomics. With my work I have established a multi-omic approach to cancer in a Rome based clinical network between Policlinico Tor Vergata Hospital and the San Carlo di Nancy Hospital, highlighting the criticalities of establishing a complex clinical-translational network. Focusing on the output of this approach, I have analysed a cohort of patients affected by kidney cancer, which would greatly benefit from a more precise molecular characterization, which might be used for treatment selection in advanced cases.

Side research activities: during my PhD I have also been involved in other research projects, on *the role of p53 in maintaining chromatin structure in a model of murine pancreatic adenocarcinoma*, during my initial year, partially based in the University of Cambridge, MRC Toxicology Unit, Leicester, UK and on the study of *p63 molecular signature in human squamous carcinomas*, during the second year of my PhD.

Finally, I have also been involved in editorial activities initially as assistant to the editorial office in Cell Death and Differentiation and Cell Death and Disease, acting as a proper Editor on Cell Death Discovery (June 2021 – present).

LIST OF PUBLICATIONS

The p53 family member p73 in the regulation of cell stress response - Biol Direct. 2021 Nov 8;16(1):23

Serine and one-carbon metabolisms bring new therapeutic venues in prostate cancer - Discov Oncology 2021

The efficacy of a medical device based on Phenolmicin P3 and Bosexil (Mictalase®) in symptoms control and prevention of lower urinary tract infections in patients undergoing Thulium Laser Enucleation of Prostate: a single-center, randomized, controlled, phase III study - Urology 2021, under evaluation

Global mapping of cancers: The Cancer Genome Atlas and beyond - Mol Oncol. 2021 Jul 10. doi: 10.1002/1878-0261.13056.

Liquid biopsies and cancer omics - Cell Death Discov. 2020 Nov 26;6(1):131. doi: 10.1038/s41420-020-00373-0.

Pathophysiology of Crohn's disease inflammation and recurrence - Biol Direct. 2020 Nov 7;15(1):23. doi: 10.1186/s13062-020-00280-5.

Cancer predictive studies - Biol Direct. 2020 Oct 14;15(1):18. doi: 10.1186/s13062-020-00274-3.

The role of noncoding RNAs in epithelial cancer - Cell Death Discov. 2020 Mar 12;6:13. doi: 10.1038/s41420-020-0247-6.