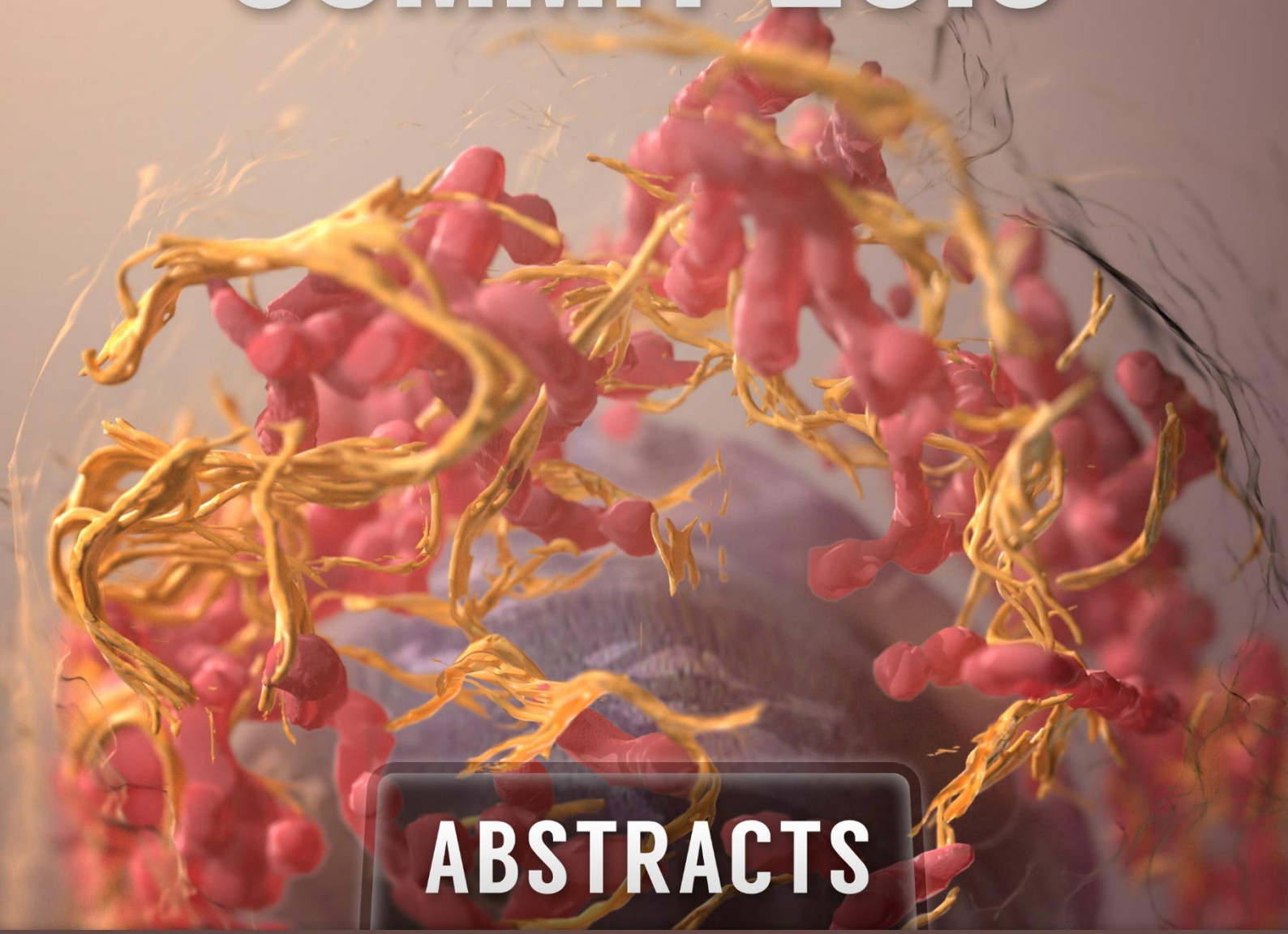
THE CONTROLLING CANCER SUMMIT 2016



ABSTRACTS

17th - 19th May 2016
London, UK

EuroSciCon

The annual Controlling Cancer Summit in an international academic event with plenty of opportunity for networking and debate. In an informal setting, this meeting will bring you up to date with current research and thinking regarding screening, prevention and treatment in this ever-growing field. Presenting at this event, we will have a variety of clinicians, academics and members of the pharmaceutical industry; we encourage presentations from the wide spectrum of cancer research, development and healthcare professionals.

This event has CPD accreditation

This abstract book will be finalised two weeks before the event
www.lifescienceevents.com/Cancer2016

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Invited Speakers Abstracts

Non-Natural Nucleosides as Therapeutic Agents Against Glioblastoma

Dr Anthony J. Berdis, Ph.D., Chair, IACUC Committee, Associate Professor of Chemistry and Biology, Cleveland State University, Cleveland, OH, USA

Brain cancers are the deadliest form of all cancers, having very low 5-year survival rates. One agent used to treat brain cancer is temozolomide that causes cell death by damaging DNA. Unfortunately, this drug is only moderately effective as resistance frequently occurs due to mutagenesis. To combat this problem, we developed a nucleoside analog that is efficiently and selectively incorporated opposite DNA lesions generated by temozolomide. This nucleoside potentiates the effects of temozolomide by inhibiting the misreplication of DNA lesions created by temozolomide. Combining our nucleosides with temozolomide provides a new and more effective therapy to treat brain cancer.

DNA repair gene polymorphisms as risk factors and chemotherapy response predictors for lung adenocarcinoma in Serbia

Miss Ivana Boljevic, Laboratory for Molecular Genetics, Institute for Oncology and Radiology of Serbia, Serbia

Different DNA repair systems maintain the integrity of the human genome. Failure to repair DNA damage leads to genomic instability and possibly cancer development. In addition to associations with cancer risk, DNA repair gene polymorphisms are candidates for affecting the efficacy of chemotherapy and survival time after cancer diagnosis. XRCC1 is a major protein involved in DNA base excision repair, while Rad51 is crucial for homologous recombination during double-strand break repair. We hypothesized that polymorphisms in these genes influence the susceptibility of individuals to lung adenocarcinoma as well as clinical outcomes among patients treated with platinum based chemotherapy in Serbian population.

The stress protein TP53INP1 plays a tumor suppressive role by regulating metabolic homeostasis

Dr. Alice Carrier, Inserm - Institut national de la santé et de la recherche médicale, Paris, France

The gene encoding the Tumor Protein 53-Induced Nuclear Protein 1 (TP53INP1) is a p53-target gene, which is over-expressed during stress events including inflammation. TP53INP1 contributes to stress responses by two different ways. First, in the nucleus, TP53INP1 regulates the transcriptional activity of p53 and p73 by direct interaction, and mediates the antioxidant activity of p53. Second, independently of p53, TP53INP1 contributes to autophagy and more particularly mitophagy. Control of cell redox status by TP53INP1 stems from its implication in mitochondrial quality control and regulation of energetic metabolism. TP53INP1 is thus a key stress protein with antioxidant-associated tumor suppressive function.

Targeted nanomedicines in cancer therapy

Dr Christine Dufes, Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK

The possibility of using genes or natural product extracts as medicines to treat cancer is limited by the lack of delivery systems able to selectively deliver these promising drugs to tumours. We demonstrated that the intravenous administration of a tumour-targeted dendriplex led to tumour disappearance of 90% of the tested A431 tumours over one month. In addition, the intravenous administration of green tea extract epigallocatechin gallate encapsulated in novel tumour-targeted vesicles resulted in complete disappearance of 40% of the tested tumour types.

Adoptive T cell Therapy for Cancer

Dr David Edward Gilham, The University of Manchester, Withington, Manchester, United Kingdom

Objective clinical responses achieved by tumour infltrating lymphocytes in malignant melanoma and engineered CAR T cells targeting B cell leukaemia demonstrate that therapy of advanced cancer by the adoptive transfer of tumour reactive T cells is both feasible and delivers potentially spectacular clinical responses in advanced chemo-resistant disease. The challenge now is to further develop the necessary technologies to permit the testing of natural and engineered T cells in the wider cancer context including 'immune-resistant' solid tumours and to establish protocols that deliver effective therapy in the absence of on-target off-tissue toxicity.

Nucleosomics®- Revolutionising Cancer Diagnostics

Dr Mark Eccleston, Business Development Director, VolitionRx, United Kingdom

Cell free nucleosomes derived from dying cancer cells provide an opportunity for novel blood-based biomarker development. The profile of epigenetic features, including histone modifications and variants, DNA modifications and adducts between nucleosomes and non-histone proteins can be correlated with clinical disease and overcomes a major limitation of simple nucleosome quantification for diagnostic and prognostic use. This talk will focus on the development of the Nucleosomics technology platform with initial data from a 14 000 prospective FIT screened colorectal cancer cohort.

CYP3A variation, hormone levels, breast cancer risk and prognosis

Dr Olivia Fletcher, Genetic Epidemiology The Institute of Cancer Research, London, United Kingdom

Epidemiological studies provide strong evidence for a role of endogenous hormones in the etiology of breast cancer. We geno¬typed single-nucleotide polymorphisms (SNPs), tagging genes involved in the synthesis and metabolism of estrogen in premenopausal women and tested for association with urinary estrone glucuronide (E1G) levels. We identified a SNP mapping to the CYP3A locus that was associated with lower E1G levels, earlier menarche and reduced breast cancer risk. Fine-mapping implicates a putative causal allele (CYP3A7*1C). Predicated on the assumption that genetically-determined effects on metabolism may impact on patient outcome, we tested this allele for association with breast cancer specific survival.

Dendritic cell derived exosomes for cancer therapy

Associate Professor Susanne Gabrielsson, Karolinska Institutet, Dept. of Medicine, Translational Immunology Unit, Stockholm, Sweden

Peptide loaded exosomes are promising cancer treatment vehicles, however, low T cell responses in human clinical trials indicate a need to further understand exosome-induced immunity. We previously demonstrated that antigen-loaded exosomes carry whole protein antigens and require B cells for induction of antigen-specific T cells. I will discuss our latest data where we investigated the need for different immune related molecules on exosomes to induce T cell responses and tumor rejection in the B16 mouse melanoma model. Our data demonstrate ways to increase the feasibility of exosome-based therapeutic approaches in cancer.

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Targeting non death domain-containing TNFR family members for cancer therapy: direct, carcinoma cell-specific death by CD40 signalling

Dr Nikolaos Georgopoulos, Department of Biological Sciences, School of Applied Sciences, University of Huddersfield, Huddersfield, United Kingdom

The role of TNFR family members in regulating cell fate has been under extensive research for decades. Due to their ability to induce cell death, death receptors represent a promising target for cancer therapy. Most studies have focused on death receptors, such as Fas and TRAIL-R, due to their strong pro-apoptotic potential in malignant cells, yet these can also be toxic to normal cells. However, cell death can be triggered via non death domain-containing TNFRs. We were the first to show that CD40 ligation by membrane ligand (mCD40L), but not soluble agonist, triggers extensive apoptosis in carcinoma cells, whilst sparing their normal counterparts, a unique property for a TNFR superfamily member. We have now identified the molecular nature of the tumour-specific CD40-signalling 'black-box' which allowed us to a) explain the differences in pro-apoptotic potential between soluble and membrane agonists, and b) design a novel combinatorial therapeutic approach that shows therapeutic efficacy.

Chromosomal instability and the metabolic constraints on cancer growth

Dr Stephen Gregory, The University of Adelaide, Adelaide, Australia

Advanced tumours frequently show defective regulation of chromosome segregation (CIN), which makes them a moving target for therapy. We use genetic approaches in Drosophila to identify inhibitors that can specifically kill these chromosomally unstable cells. Our data suggest that CIN cells are highly sensitive to any perturbation that increases glycolytic flux or mitochondrial membrane potential; such changes lead to the production of Reactive Oxygen Species (ROS), DNA damage and apoptosis. Our latest data on a tumour explant model will be presented, showing the metabolic constraints on CIN tumour growth and possible interventions.

Therapeutic targeting of erbB3 receptor for cancer treatment

Associate Professor Bolin Liu, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

ErbB3 receptor functions as a major cause of treatment failure in cancer therapy. Although inhibition of erbB3 is required to enhance cancer therapeutic efficacy, to date no erbB3-targeted therapy has been approved for cancer treatment. We show that the anti-erbB3 Ab MM-121 abrogates trastuzumab- and paclitaxel-resistance against erbB2-positive breast cancer. Our recent data support that effective inhibition/downregulation of erbB3 can also be achieved by an HDAC inhibitor and functional cooperative miRNAs. This novel epigenetic approach targeting of erbB3 may eliminate the chance for tumor cells to develop resistance after initial response, and thus have a significant impact on cancer therapy.

The antitumor activity of cannabinoids in colorectal cancer

Dr David Meiri, Technion-Israel Institute of Technology, Haifa, Israel

Colorectal cancer (CRC) is considered to be one of the most common forms of malignancy. During the past decade, significant strides have been made in our understanding of the biology of CRCs and the prognosis for CRC patients has been steadily improving. However, despite these recent advances, CRC often results in mortality, thus underscoring the importance of elucidating novel and fresh strategies for the treatment of CRC.

Recently, the therapeutic potential of phytocannabinoids, the unique active compounds of the plant Cannabis, has been rediscovered in the area of cancer research. More than 100 phytocannabinoids have been identified within the Cannabis plant. A few specific

cannabinoids have been proposed as having therapeutic potential for various diseases, including cancer.
In this study we establish the antitumor consequences of different cannabinoids on CRCs. Our preliminary data indicate that cannabis extracts have the capacity to inhibit CRC cell growth. However, the magnitude of this inhibition is dependent upon the specific cannabis strain.

The surface and shape of the breast cancer tumors and its relationship with lymph node metastases

Dr Marcel Segura Badia, Hospital del Mar. Autonomous University of Barcelona, Barcelona, Spain

In breast cancer, TNM staging is very important to perform accurated prognosis, choose the best treatment and make comparable studies. However, T only tell us about the maximum diameter, neglecting factors as the tumor shape and, therefore, its surface. This can give us more information about the probability to suffer nodal metastasis than the diameter, being that metastasis is more likely in surface tumor cells. In this study we try to ascertain which one of both methods (maximum diameter or tumor surface) give us more accurated and reliable information about breast cancer tumors.

Precious metals for cancer treatment - a novel approach

Dr. Isolda Romero-Canelón, University of Warwick, Coventry, United Kingdom

DNA methylation in epithelial-to-mesenchymal transition

Dr. Bozena Smolkova, Cancer Research Institute of Slovak Academy of Sciences, Bratislava, Slovakia

In a majority of cancers, including breast cancer, mortality is caused by metastases rather than primary tumours. Genesis of metastases is believed to be preceded by dissemination of tumour cells into the blood circulation or lymphatic channels, which is determined by their morphological and functional dedifferentiation from the epithelial to mesenchymal phenotype. This complex process, known as epithelial-to-mesenchymal transition (EMT), leads to an increased motility and loss of cell adhesion. The genome-wide loss of DNA methylation accompanied by gene specific hypermethylation is regarded as a common epigenetic event in malignancies and may play crucial roles in carcinogenesis, including regulation of EMT processes and subsequent metastatic spread. However EMT-related epigenetic alterations are still poorly understood.

Targeted delivery of potential therapeutics in glioblastoma

Dr Amanda Tivnan, Royal College of Surgeons in Ireland, Dublin, Ireland

Glioblastoma is a highly aggressive brain cancer representing approximately 17% of all primary brain tumours diagnosed worldwide. A major hindrance to eliciting effective GBM treatment is inefficient transport across the blood-brain barrier (B-BB) and drug extrusion at the cancer cell surface. Dr. Tivnan discusses the use of RNA interference-mediated inhibition of ABC-transporters to improve drug response in GBM cells, facilitated through encapsulation of short interfering RNA within surface-modified poly(lactic-co-glycolic acid (PLGA) nanoparticles. To ensure GBM cell specific delivery, the surface of PLGA nanoparticles are modified to allow targeted delivery to brain cancer cells, reducing off-target treatment effects.

OMICS biomarkers and their implication in cancer control

Dr Mukesh Verma, Methods and Technologies Branch Program Director. Epidemiology and Genomics Research Program, National Institutes of Health (NIH), USA

Precision medicine is an emerging science with the potential to improve early cancer diagnosis and enable the development of treatment based on an individual's genetic background, family history, and other characteristics. Identifying patients who may benefit from personalized and precision therapy depends on identifying accurate assays for the biomarkers that are needed to determine optimal treatment. Compared to the rapid progress in technology development, the progress in treatment timing has been slow. Most clinicians rely on pathology reports that become available in due time, which often is too late to control or treat cancer. Molecular profiling (mostly omics profiling based on genomics, metabolomics, epigenomics, transcriptomics, and glycomics data) and molecular classification of cancer can be achieved in real time and may help to identify those cancer-associated biomarkers that are expressed much earlier than pathological symptoms and characteristics appear in histopathological analyses. Once these biomarkers are included in personalized medicine, it will enable treatment to be implemented earlier, which will produce better outcomes. Although the traditional approach to personalized medicine has been "reactive" in the future, it will be "Proactive."
Research Questions discussed during presentation include:

- Identifying targets of therapy from profiling of genomics, epigenomics, metabolomics, and transcriptomics and integrate them in clinical practice
- Combining molecular pathology data with omics data to reduce false positive results
- Develop new algorithms based on molecular profiling and make novel risk prediction models
- Integrate microbiome data with omics data to help develop new screening and risk prediction tools
- Apply precision medicine to identify individuals/populations who will response to treatment
- Develop cost-effective companion diagnostic texts based on omics profiling

Targeting the tumour microenvironment in anti-cancer therapy

Professor Kaye Williams, University of Manchester, Manchester Pharmacy School, Manchester, United Kingdom

Tumours have a complex microenvironment. Complexity comes from physiological and environmental stresses such as hypoxia (low oxygen supply), nutrient deprivation and acidosis and from the multiple cell types that contribute to the overall tumour tissue. The latter includes endothelium, stromal and inflammatory cell components. All of these cell types play important roles in tumour growth and can be direct targets of anti-cancer therapies. Importantly the tumour microenvironment and comprising cells can also influence how the tumour responds to therapies that are targeted at different facets of tumour cell biology. This will be the focus of the presentation.

DNA damage repair and p53 gene in platinum-drug resistance

Dr Jing Jie Yu, Mary Babb Randolph Cancer Center, West Virginia University, Morgantown, WV, United States

Tumor drug resistance remains a major obstacle in the treatment of cancers. p53, Chk2 and ERCC1 of the DNA damage/repair pathway were activated after cells were exposed to cisplatin or dicycloplatin. Overexpression of p53 in wt-p53 (but not p53-deficient) cells doubled Chk2 phosphorylation. p53 knockdown greatly reduced Chk2 phosphorylation, indicating that wild-type p53, in response to platinum-drugs, plays a role in the upstream regulation of the DNA-adduct repair pathway and mediates acquired platinum resistance. We strongly suggest that it is important to include p53 mutational status in any p53-involved studies due to the functional differentiation of wt-p53 and p53-mutant.

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Day 1:

Oral Presentation Abstracts

Oral presentations will be added after the submission deadline

Day 2:

Oral Presentation Abstracts

WNT SIGNALLING PATHWAY IS TARGETED IN MENINGIOMA

Nives Pećina-Šlaus[1,2] , Anja Kafka[1,2], Josip Skoko[1,3], Monika Logara[1], Niko Njirić[1], Davor Tomas[4,5]

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Meningiomas which originate from the arachnoidal cap cells of the leptomeninges account for approximately 30% of primary intracranial and intraspinal neoplasms. The molecular mechanisms, signaling pathways and candidate genes involved in their development still need elucidation. In the present study we investigated the involvement of Wnt signaling pathway in meningioma by analyzing its key molecules, beta-catenin, APC, DVL3, AXIN1 and E-cadherin. The chosen pathway is well known for its role in development and tumorigenesis. Genetic changes of tumor suppressor genes APC, E-cadherin (CDH1) and AXIN1 were analyzed by PCR/loss of heterozygosity (LOH). Multiplex PCR was used for DVL3 analysis. The expression and cellular localizations of proteins were investigated by immunohistochemistry. The results obtained on APC showed 47% of meningiomas with LOH of this gene. Immunostaining showed that samples with LOHs were accompanied with the absence of APC protein expression or presence of mutant APC proteins (Chi square =13.81, df = 2, P<0.001). Immunostaining showed that beta-catenin was upregulated and transferred to the nucleus in 71,2% of meningiomas. This high frequency is indicative of oncogenic activation of Wnt signaling. We also showed that nuclear localization of beta-catenin correlates to gross deletions of APC gene (Chi square =21,96, df = 2, P<0.0001). Downregulation or loss of E-cadherin expression was observed in 58% of samples and gross deletions (LOH) of this gene were found in 32% of meningiomas. Our findings demonstrated that there was significant association between the genetic changes of CDH1 and the nuclear localization of beta-catenin protein (Chi square =5,25, df =1, P<0,022). Loss of E-cadherin and beta-catenin's translocation to the nucleus are two prominent features of epithelial to mesenchymal transition, a process involved in invasion and metastasis of tumors. LOH of AXIN1 gene was observed in 21.1% of meningiomas and AXIN1 expression levels were negative or very weak in 21.9% of meningiomas. All the other samples had AXIN1 localized in both the cytoplasm and nucleus with moderate expression in 34.4% and

strong in 43.8%. DVL3 was amplified in 23,81% of analyzed samples. Microsatellite instability (MSI), the result of impaired cellular mismatch repair, was also detected, MSI for CDH1 gene in 11%, for DVL3 in 9,52% and for AXIN1 in 5.3% of investigated meningiomas. Our results suggest that Wnt signaling pathway plays important role in meningioma. The ongoing research is aiming to offer new molecular markers for meningioma based on the genetic pathways and molecules involved and help to develop new treatment modalities.

Day 3:

Oral Presentation Abstracts

Oral presentations will be added after the submission deadline

Poster Presentation Abstracts

Poster abstracts will be finalised weeks before the event

BARRIERS TO BREAST CANCER SCREENING AMONG WOMEN IN JEDDAH, SAUDI ARABIA

A. Alzahrani, *H. Alraddadi*, A. Alsehly
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Introduction and Research Problem: In Saudi Arabia, breast cancer is the most common cancer among both sexes and all age groups. Breast cancer mortality rates have steadily been decreasing worldwide, with advances in screening programs being key to early detection and treatment. Literature points to very low screening rates in the Kingdom of Saudi Arabia. We aimed to understand what barriers may prevent Saudi women living in the city of Jeddah from early detection screening.

Materials and Methods: A cross sectional study was conducted via inter-personal surveys, across various public locations in Jeddah, Saudi Arabia. With an estimated population of 491,678 Saudi females aged more than 20 years of age in the city of Jeddah, the sample required with a confidence interval of 95% and a 5% margin of error was 384 females.

Summary of Results: 421 women participated in the survey. They were aged twenty and above, clustered into six age groups. The most common barrier was “I didn’t know I’m supposed to screen for breast cancer”, with a frequency of 149 (35%); followed by difficulty with appointments (21%), and embarrassment (16%). Only 54 women (12.8%) reported regular check-up with a family or general physician.

Conclusion: Our findings highlight a wanting need for national breast cancer awareness campaigns. Lack of knowledge regarding screening protocols, especially among younger age groups, must be addressed by widespread national campaigns targeted at raising awareness towards screening options and availability. Orienting the public to the importance of primary healthcare and regular follow up, even when not ill, is crucial to promoting health awareness and early detection screening.

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