

## SELECTED ABSTRACTS FROM PUBMED

1. **Praharaj PP, Bhutia SJ, Nagrath S, Bitting RL, Deep G. Circulating tumor cell-derived organoids: Current challenges and promises in medical research and precision medicine. *Biochim Biophys Acta Rev Cancer*. 2018 Apr;1869(2):117-127.**

### ABSTRACT

Traditional 2D cell cultures do not accurately recapitulate tumor heterogeneity, and insufficient human cell lines are available. Patient-derived xenograft (PDX) models more closely mimic clinical tumor heterogeneity, but are not useful for high-throughput drug screening. Recently, patient-derived organoid cultures have emerged as a novel technique to fill this critical need. Organoids maintain tumor tissue heterogeneity and drug-resistance responses, and thus are useful for high-throughput drug screening. Among various biological tissues used to produce organoid cultures, circulating tumor cells (CTCs) are promising, due to relative ease of ascertainment. CTC-derived organoids could help to acquire relevant genetic and epigenetic information about tumors in real time, and screen and test promising drugs. This could reduce the need for tissue biopsies, which are painful and may be difficult depending on the tumor location. In this review, we have focused on advances in CTC isolation and organoid culture methods, and their potential applications in disease modeling and precision medicine.

**Keywords:** Cancer; Circulating Tumor Cells; Organoids; Precision Medicine.

2. **Ha TC, Ng S, Chen C, Yong SK, Koh GCH, Tan SB, Malhotra R, Altermatt F, Seim A, Biderman A, Woolley T, Østbye T. Inclination towards research and the pursuit of a research career among medical students: an international cohort study. *BMC Med Educ*. 2018 May 2;18(1):86.**

### ABSTRACT

**Background:** Involvement of clinicians in biomedical research is imperative for the future of healthcare. Several factors influence clinicians' inclination towards research: the medical school experience, exposure to research article reading and writing, and knowledge of research. This cohort study follows up medical students at time of graduation to explore changes in their inclination towards research and pursuing a research career compared to their inclination at time of entry into medical school.

**Methods:** Students from medical schools in six different countries were enrolled in their first year of school and followed-up upon graduation in their final year. Students answered the same self-administered questionnaire at both time points. Changes in inclination towards research and pursuing a research career were assessed. Factors correlated with these changes were analysed.

**Results:** Of the 777 medical students who responded to the study questionnaire at entry into medical school, 332 (42.7%) completed the follow-up survey. Among these 332 students, there was no significant increase in inclination towards research or pursuing a research career over the course of their medical schooling. Students from a United States based school, in contrast to those from schools other countries, were more likely to report having research role models to guide them (51.5% vs. 0%-26.4%) and to have published in a peer-reviewed journal (75.7% vs. 8.9%-45%). Absence of a role model was significantly associated with a decrease in inclination towards research, while an increased desire to learn more about statistics was significantly associated with an increase in inclination towards pursuing a research career.

**Conclusion:** Most medical students did not experience changes in their inclination towards research or pursuing a research career over the course of their medical schooling. Factors that increased their inclination to undertaking research or pursuing a research career were availability of a good role model, and a good knowledge of both the research process and the analytical tools required.

**Keywords:** Cohort; Inclination; Medical students; Research; Research Career.

3. **Zhang S, Duan E. Fighting against Skin Aging: The Way from Bench to Bedside. *Cell Transplant*. 2018 May;27(5):729-738.**

### ABSTRACT

As the most voluminous organ of the body that is exposed to the outer environment, the skin suffers from both intrinsic and extrinsic aging factors. Skin aging is characterized by features such as wrinkling, loss of elasticity, laxity, and rough-textured appearance. This aging process is accompanied with phenotypic changes in cutaneous cells as well as structural and functional changes in extracellular matrix components such as collagens and elastin. In this review, we summarize these changes in skin aging, research advances of the molecular mechanisms leading to these changes, and the treatment strategies aimed at preventing or reversing skin aging.

**Keywords:** Extracellular Matrix; Extrinsic Aging; Intrinsic Aging; Skin Aging; Treatment Strategy.

4. **Seehusen DA, Mainous AG 3rd, Chessman AW. Creating a Centralized Infrastructure to Facilitate Medical Education Research. *Ann Fam Med*. 2018 May;16(3):257-260.**

### ABSTRACT

**Purpose:** Building research capacity and increasing scholarly productivity are identified needs of the specialty of family medicine. The Accreditation Council for Graduate Medical Education (ACGME) has increased the scholarly requirements for residency programs, placing even more

pressure on faculty to be productive in the scholarly realm. The Council of Academic Family Medicine Educational Research Alliance (CERA) was created by volunteer members of the specialty with shared interests in overcoming barriers and increasing scholarly production.

**Methods:** CERA has developed the infrastructure and expertise to regularly conduct omnibus surveys of key family medicine educational leaders. Proposals are centrally collected and competitively chosen. The omnibus survey process includes collaboration with experienced mentors, centralized institutional review board clearance, pilot testing, and centralized data collection. The survey results are disseminated back to research teams for presentation and publication of the findings.

**Results:** To date, over 115 research teams have had their projects included in CERA omnibus surveys. Projects have been led by research teams from across the country and with a wide variety of research experience. This collaborative work has resulted in more than 75 scientific presentations and over 55 peer-reviewed papers in the medical literature. The raw data are now available online and serve as a repository for future secondary analysis and as an educational resource.

**Conclusions:** The CERA infrastructure has allowed a large number of research teams to conduct meaningful scholarship at a fraction of the typical cost in terms of time and energy. CERA has expanded family medicine research by removing barriers for teams with limited experience or resources.

**Keywords:** Primary Care Research; Research Capacity.

5. **Hemingway H, Asselbergs FW, Danesh J, Dobson R, Maniadakis N, Maggioni A, van Thiel GJM, Cronin M, Brobert G, Vardas P, Anker SD, Grobbee DE, Denaxas S; Innovative Medicines Initiative 2nd programme, Big Data for Better Outcomes, BigData@Heart Consortium of 20 academic and industry partners including ESC. Big data from electronic health records for early and late translational cardiovascular research: challenges and potential. Eur Heart J. 2018 Apr 21;39(16):1481-1495.**

#### ABSTRACT

**Aims:** Cohorts of millions of people's health records, whole genome sequencing, imaging, sensor, societal and publicly available data present a rapidly expanding digital trace of health. We aimed to critically review, for the first time, the challenges and potential of big data across early and late stages of translational cardiovascular disease research.

**Methods and results:** We sought exemplars based on literature reviews and expertise across the BigData@Heart Consortium. We identified formidable challenges including: data quality, knowing what data exist, the legal and ethical framework for their use, data sharing, building and maintaining public trust, developing standards for defining disease, developing tools for scalable, replicable science and equipping the clinical and scientific work force with new

inter-disciplinary skills. Opportunities claimed for big health record data include: richer profiles of health and disease from birth to death and from the molecular to the societal scale; accelerated understanding of disease causation and progression, discovery of new mechanisms and treatment-relevant disease sub-phenotypes, understanding health and diseases in whole populations and whole health systems and returning actionable feedback loops to improve (and potentially disrupt) existing models of research and care, with greater efficiency. In early translational research we identified exemplars including: discovery of fundamental biological processes e.g. linking exome sequences to lifelong electronic health records (EHR) (e.g. human knockout experiments); drug development: genomic approaches to drug target validation; precision medicine: e.g. DNA integrated into hospital EHR for pre-emptive pharmacogenomics. In late translational research we identified exemplars including: learning health systems with outcome trials integrated into clinical care; citizen driven health with 24/7 multi-parameter patient monitoring to improve outcomes and population-based linkages of multiple EHR sources for higher resolution clinical epidemiology and public health.

**Conclusion:** High volumes of inherently diverse ('big') EHR data are beginning to disrupt the nature of cardiovascular research and care. Such big data have the potential to improve our understanding of disease causation and classification relevant for early translation and to contribute actionable analytics to improve health and healthcare.

6. **Patch C, Middleton A. Genetic counselling in the era of genomic medicine. Br Med Bull. 2018 Jun 1;126(1):27-36.**

#### ABSTRACT

**Background:** Genomic technology can now deliver cost effective, targeted diagnosis and treatment for patients. Genetic counselling is a communication process empowering patients and families to make autonomous decisions and effectively use new genetic information. The skills of genetic counselling and expertise of genetic counsellors are integral to the effective implementation of genomic medicine.

**Sources of data:** Original papers, reviews, guidelines, policy papers and web-resources.

**Areas of agreement:** An international consensus on the definition of genetic counselling. Genetic counselling is necessary for implementation of genomic medicine.

**Areas of controversy:** Models of genetic counselling.

**Growing points:** Genomic medicine is a growing and strategic priority for many health care systems. Genetic counselling is part of this.

**Areas timely for developing research:** An evidence base is necessary, incorporating implementation and outcome research, to enable health care systems, practitioners,

patients and families to maximize the utility (medically and psychologically) of the new genomic possibilities.

7. **Starr S. How to talk about genome editing. Br Med Bull. 2018 Jun 1;126(1):5-12.**

#### ABSTRACT

**Background:** Human genome editing is an area of growing prominence, with many potential therapeutic applications.

**Sources of data:** A project by two UK charities, whose participants included fertility sector patients and practitioners and also people affected by genetic disease and rare disease. Scientific research into, and wider discussion of, genomics and genome editing.

**Areas of agreement:** There is a need for improved public and professional understanding of genome editing.

**Areas of controversy:** The way genome editing is discussed is often inconsistent and confusing. Simply defining and explaining the term 'genome' can present challenges.

**Growing points:** There are approaches that lend themselves to achieving greater clarity and coherence in discussion of genome editing.

**Areas timely for developing research:** People's understanding should ideally be able to withstand and evolve alongside current developments in genome editing, rather than being tied firmly to specific aspects of genome editing (which may in future be supplanted).

8. **Jensen LB, Kyvik KO, Leth-Larsen R, Eriksen MB. Research integrity among PhD students within clinical research at the University of Southern Denmark. Dan Med J. 2018 Apr;65(4):A5469.**

#### ABSTRACT

**Introduction:** Responsible conduct of research is the basis for the credibility of all research. Research misconduct is defined as the fabrication, falsification or plagiarism committed willfully or grossly negligently in the planning, performing or reporting of research. We undertook a survey of knowledge of the attitudes towards and experiences with research misconduct among PhD students in clinical research.

**Methods:** A questionnaire previously used in Swedish and Norwegian studies was distributed to PhD students (n = 330) affiliated with the Department of Clinical Research or Department of Regional Health Research, University of Southern Denmark.

**Results:** A total of 165 PhD students completed the questionnaire in full or in part, yielding an overall response rate of 50%. 18-34% reported to have heard (within the past year) about researchers who had plagiarised, falsified or fabricated data, or plagiarised publications. None reported this to occur in their own department. Few stated that they had felt under pressure to either falsify data (1%) or present results in a misleading way (3%). However, 22% stated to

have felt an unethical pressure (within the past year) regarding the inclusion or order of authors.

**Conclusions:** Results indicate that, albeit at a low frequency, research misconduct involving PhD students is taking place. Likewise, a high fraction of respondents reported to have been under pressure regarding authorships, which points to questionable research practices in clinical research.

9. **Burz C, Pop VV, Buiga R, Daniel S, Samasca G, Aldea C, Lupan I. Circulating tumor cells in clinical research and monitoring patients with colorectal cancer. Oncotarget. 2018 May 11;9(36):24561-24571.**

#### ABSTRACT

Colorectal cancer remains a frequent disease to which screening and target therapy exist, but despite this is still marked by a high mortality rate. Even though radical surgery may be performed in many cases, patients relapse with metastatic disease. Circulating tumor cells were incriminated for tumor recurrence, that's why vigorous research started on their field. Owing prognostic and predictive value, it was revealed their usefulness in disease monitoring. Moreover, they may serve as liquid biopsies for genetic tests in cases where tissue biopsy is contraindicated or cannot be performed. In spite of these advantages, they were not included in clinical guidelines, despite CellSearch and many other detection methods were developed to ease the identification of circulating tumor cells. This review highlights the implication of circulating tumor cells in metastasis cascade, intrinsic tumor cells mechanisms and correlations with clinical parameters along with their utility for medical practice and detection techniques.

**Keywords:** Circulating Tumor Cells; Colorectal Cancer; Metastasis; Prognostic Factor; Survival.

10. **Chin-Yee B, Subramanian SV, Verma AA, Laupacis A, Razak F. Emerging Trends in Clinical Research: With Implications for Population Health and Health Policy. Milbank Q. 2018 Jun;96(2):369-401.**

#### ABSTRACT

**Policy Points:** Significant advances in clinical medicine that have broader societal relevance may be less accessible to population health researchers and policymakers because of increased specialization within fields. We describe important recent clinical advances and discuss their broader societal impact. These advances include more expansive strategies for disease prevention, the rise of precision medicine, applications of human microbiome research, and new and highly successful treatments for hepatitis C infection. These recent developments in clinical research raise important issues surrounding health care costs and equitable resource allocation that necessitate an ongoing dialogue among the fields of clinical medicine, population health, and health policy.

**Context:** Developments in clinical medicine have important implications for population health, and there is a need for

interdisciplinary engagement among clinical medicine, the social sciences, and public health research. The aim of this article is to help bridge the divide between these fields by exploring major recent advances in clinical medicine that have important implications for population health.

**Methods:** We reviewed the most cited articles published from 2010 to 2015 in 5 high-impact clinical journals and selected 5 randomized controlled trials and 2 related clinical practice guidelines that are broadly relevant to population health and policy.

**Findings:** We discuss the following themes: (1) expanding indications for drug therapy and the inherent medicalization of the population as highlighted by studies and clinical guidelines supporting lower blood pressure targets or widespread statin use; (2) the tension in nutritional research between quantifying the impact of isolated nutrients and studying specific foods and dietary patterns, for example,

the role of the Mediterranean diet in the primary prevention of cardiovascular disease; (3) the issue of high medication costs and the challenge of providing equitable access raised by the development of new and effective treatments for hepatitis C infection; (4) emerging clinical applications of research on the human microbiome as illustrated by fecal transplant to treat *Clostridium difficile* infections; and (5) the promise and limitations of precision medicine as demonstrated by the rise of novel targeted therapies in oncology.

**Conclusions:** These developments in clinical science hold promise for improving individual and population health and raise important questions about resource allocation, the role of prevention, and health disparities.

**Keywords:** Clinical Trials; Drug Costs; Health Equity; Public Health; Social Sciences.