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Interview

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Feature interview with Dr. William C. CHO - "Clarivate 2023 Highly Cited Researcher"

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Abstract

This insightful interview article covers the *Journal of Cancer Metastasis and Treatment*'s special interview with Dr. William C. Cho, focusing on his career trajectory, research focus, and ambitious goals for the next five years in cancer research. Dr. Cho, recognized as a Highly Cited Researcher in 2023 by Clarivate, has a wide research spectrum, including cancer biomarkers, non-coding RNA, genomics, and bioinformatics. In the interview, he elaborates on how advancements in these areas contribute to cancer treatment, emphasizing their potential impact on personalized medicine and therapeutic strategies. Dr. Cho shares experiences, underscores the importance of interdisciplinary collaborations, and highlights upcoming trends in cancer research. The interview may offer some guidance and advice to early-career researchers, encouraging them to find their passion, broaden their horizons, and make meaningful contributions to the field of cancer research.

INTRODUCTION

On December 20, 2023, the Editorial Office of *Journal of Cancer Metastasis and Treatment* (*JCMT*) had the privilege of conducting a special interview with one of the Editorial Board members, Dr. William Cho [Figure 1]. He is leading a Special Issue "The Emerging Role of Extracellular Vesicles in Cancer" for *JCMT*.

Figure 1. Dr. William C. CHO.

Dr. William C. Cho has been recognized as "Highly Cited Researchers for 2023" by Clarivate. He is a Chartered Scientist (UK), and Fellow Member of several institutes, including the Institute of Biomedical Science (UK), Hong Kong Institute of Biomedical Science, and Hong Kong Society for Molecular Diagnostic Sciences. Dr. Cho's research endeavors focus on cancer biomarkers, non-coding RNA, genomics, proteomics, next-generation sequencing, bioinformatics, meta-analysis, *etc.* His prolific contributions include over 600 peer-reviewed papers (*Lancet, Lancet Oncology, Annals of Oncology, Lancet Gastroenterology & Hepatology, JAMA Oncology, Advanced Science, Nature Communications, PNAS, Molecular Cancer, Journal of Thoracic Oncology, Journal of the National Cancer Institute, Journal of Extracellular Vesicles*, *eClinicalMedicine*, *Science Advances, Theranostics*, *Clinical Cancer Research, Clinical Chemistry, etc.*) covering cancer biomarkers, proteomics, non-coding RNA, traditional Chinese medicine, and dozens of books (including "An Omics Perspective on Cancer Research", "MicroRNAs in Cancer Translational Research", "Drug Repurposing in Cancer Therapy: Approaches and Applications" and "Resistance to Anti-CD20 Antibodies and Approaches for Their Reversal", *etc.*), and have received a citation count surpassing 28,000.

During the interview, Dr. Cho delved into his career motivations, detailed his research journey, and shared valuable experiences. Additionally, he offered insights into trending research topics while outlining his ambitious research goals for the next five years.

Hosting this interview is Dr. Suman Dutta, a member of the *JCMT*'s Junior Editorial Board, and a neurodegenerative disease research scientist at the University of California Los Angeles (UCLA). Dr. Dutta's primary research focuses on comprehending disease mechanisms and developing diagnostic tools. Presently, he is actively engaged in research initiatives at Oxford University.

THE INTERVIEW

The interview with Dr. William C. Cho encompasses a series of questions divided into five parts. Below are the intriguing highlights of the interview:

Could you highlight some key moments and pivotal turning points that have shaped your career trajectory in cancer research?

I embarked on my research endeavors focusing on nasopharyngeal carcinoma (NPC), specifically investigating the presence of Epstein-Barr virus latent membrane protein-1 in the cell-free sera of patients with NPC who experienced distant or loco-regional relapses, while observing its absence in those in complete remission. In the era of proteomics, I pursued the utilization of surface-enhanced laser desorption ionization time-of-flight mass spectrometry technology and dedicated myself to proteomic profiling using this advanced platform through hands-on experimentation during my time in the United States. The process of discovering the proteins and peptides associated with various diseases was captivating, and I first reported several intriguing biomarkers for NPC, lung cancer, and diabetes mellitus. Notably, I gained valuable experience from 2012 to 2016 as a Senior Executive responsible for evaluating scientific research proposals for health and medical research fund applications at the Food and Health Bureau (Hong Kong SAR). Overseeing diverse medical studies broadened my perspective, enhancing my ability to assimilate and synthesize ideas effectively. Returning to the laboratory subsequently amplified my research output, with several dozen papers being published annually and garnering substantial citations. Consequently, I have been acknowledged as one of the top 2% most influential scientists globally since 2017. Through unwavering dedication, I am honored to have been included in the Highly Cited Researchers list for 2023 by Clarivate.

What inspired you to focus on these specific areas, and how do you see them contributing to advancements in cancer treatment?

The rapid evolution and vibrant landscape of research, notably within oncology, have been pivotal in guiding my focus towards specific areas instrumental in progressing cancer treatment. Technological advancements have facilitated my research concentration on specific areas that contribute to advancements in cancer treatment, including cancer biomarkers, non-coding RNA, genomics, and bioinformatics:

Cancer biomarkers

The drive behind studying cancer biomarkers stems from the need for improved diagnostic and prognostic tools. Biomarkers are measurable biological indicators that can provide information about the presence, progression, or response to treatment of cancer. By identifying and studying specific molecules, such as proteins or genetic markers, researchers aim to refine methods for early detection, monitoring treatment efficacy, and predicting patient outcomes. This knowledge opens avenues for personalized treatment approaches, optimizing the selection of therapies and ultimately improving patient outcomes.

Non-coding RNA

Non-coding RNA molecules, such as microRNAs and long non-coding RNAs, have gained attention due to their regulatory roles in gene expression and cellular processes. Research in this area aims to understand the functions and mechanisms of non-coding RNAs and their involvement in cancer development and progression. By exploring their interactions with target genes and signaling pathways, researchers can identify potential therapeutic targets and develop RNA-based interventions. Non-coding RNA research contributes to the expanding field of RNA therapeutics and holds promise for novel cancer treatment strategies.

Genomics

The motivation behind genomics research in cancer revolves around unraveling the genomic alterations and variations associated with cancer initiation, progression, and response to treatment. Genomic studies, including whole-genome sequencing, transcriptomics, and epigenomics, provide comprehensive insights into the genetic landscape of cancers. These studies facilitate the identification of genetic mutations, driver alterations, and molecular subtypes of cancer. Genomic information enables the development of targeted

therapies, personalized medicine approaches, and the identification of biomarkers for treatment response prediction and patient stratification.

Bioinformatics

Bioinformatics assumes a crucial role in cancer research by furnishing computational tools and methods to analyze and interpret large-scale biological data. The motivation behind bioinformatics research in cancer is the need to extract meaningful insights from complex and diverse datasets, such as genomics, transcriptomics, proteomics, and clinical data. By leveraging computational algorithms, statistical modeling, and machine learning techniques, bioinformatics aids in identifying disease-associated patterns, predicting treatment responses, discovering new drug targets, and conducting large-scale data integration. Bioinformatics empowers researchers to make data-driven decisions and accelerate discoveries in cancer research and treatment.

The areas of cancer biomarkers, non-coding RNA, genomics, and bioinformatics are interconnected and complementary. The insights gleaned from studying cancer biomarkers, non-coding RNA, and genomic alterations converge with bioinformatics approaches, fostering a deeper understanding of cancer biology and its implications for treatment. Collectively, these fields drive advancements in precision medicine, targeted therapies, and the development of novel diagnostic and therapeutic strategies in cancer treatment. They hold the potential to improve patient outcomes, increase the effectiveness of treatments, and ultimately contribute to the goal of reducing the burden of cancer.

Over the course of your extensive research journey, could you highlight one or two particularly memorable or challenging experiences that significantly influenced your approach to scientific inquiry or altered your perspectives on cancer research?

Engaging in collaborative and interdisciplinary research projects has broadened my perspectives and challenged traditional approaches. Collaborations with clinicians, scientists from other disciplines, or industry partners offer unique insights, expertise, and resources. These experiences can foster innovative thinking, encourage the integration of different research methodologies, and lead to transformative discoveries.

Given your extensive publication record and contributions to academic books, how have interdisciplinary collaborations played a role in your research, and what advice do you have for researchers seeking to engage in collaborative projects across diverse domains?

I would like to provide some insights into the role of interdisciplinary collaborations in research and provide advice for researchers seeking to engage in collaborative projects across diverse domains:

Broadening perspectives

Interdisciplinary collaborations bring together researchers from different disciplines, such as biology, chemistry, computer science, or social sciences, to address complex research questions. These collaborations provide opportunities to gain new perspectives, insights, and approaches that may not be readily apparent within a single discipline. By combining expertise from diverse fields, researchers can develop more holistic and innovative solutions to complex problems.

Tackling complex challenges

Many research challenges in cancer and other fields require a multidimensional approach. Interdisciplinary collaborations enable researchers to combine their unique expertise and methodologies to tackle these complex challenges. Integrating different disciplinary perspectives can lead to novel insights, more comprehensive data analysis, and a better understanding of the broader implications of research findings.

Fostering creativity and innovation

Collaborating with researchers from diverse domains can spark creativity and innovation. It encourages thinking beyond traditional boundaries and allows for the exploration of unconventional ideas and approaches. Shared knowledge, skills, and perspectives can lead to breakthroughs and advancements that may not have been possible within a single discipline.

Effective communication and collaboration

Successful interdisciplinary collaborations require effective communication and collaboration skills. Researchers must bridge disciplinary jargon and communicate ideas in a way that is accessible to collaborators from different domains. Active listening, open-mindedness, and a willingness to learn from others' expertise are essential. Establishing clear goals, roles, and responsibilities, as well as maintaining regular communication, can enhance collaboration and ensure productive outcomes.

Building trust and relationships

Interdisciplinary collaborations thrive on trust and mutual respect among collaborators. It takes time to build trust, especially when working across diverse domains with different research cultures and methodologies. Engage in open and respectful discussions, value diverse perspectives, and acknowledge the expertise and contributions of each collaborator. Building strong relationships is key to long-term successful collaborations.

Seek funding opportunities and support

Collaborative projects often require additional resources and funding. Explore funding opportunities that specifically encourage interdisciplinary research. Many funding agencies recognize the value of interdisciplinary collaborations and provide grants to support such projects. Seek institutional support, establish interdisciplinary research centers or initiatives, and engage in networking events to connect with potential collaborators.

Embrace continuous learning

Engaging in interdisciplinary collaborations requires a willingness to learn and adapt. Be open to acquiring new knowledge, methodologies, and approaches from other disciplines. Attend interdisciplinary conferences or workshops, participate in training programs, and engage in self-directed learning to expand your interdisciplinary skill set and stay updated with advancements in relevant fields.

Interdisciplinary collaborations have the potential to produce groundbreaking research outcomes by leveraging the strengths of different disciplines. By embracing these collaborations, researchers can broaden their perspectives, foster innovation, and tackle complex challenges in cancer research and beyond.

With your expertise in cancer research, what do you perceive as the most promising or exciting emerging trends or technologies that have the potential to revolutionize the field in the near future?

Here are several noteworthy trends and technologies in cancer research that possess the potential to bring about a revolutionary impact in the field:

Immunotherapy and combination strategies

Immunotherapy has gained significant attention in recent years for its potential in cancer treatment. It utilizes the immune system to recognize and attack cancer cells. Approaches like immune checkpoint inhibitors, chimeric antigen receptor (CAR) T-cell therapy, and cancer vaccines have shown remarkable results, leading to long-term remission and improved survival rates. Additionally, CAR-natural killer (NK)

cell therapy combines CARs' specificity with the innate cytotoxicity of NK cells, offering a promising alternative to CAR-T cell therapy with potential benefits such as overcoming limitations associated with CAR-T therapy. To further improve immunotherapies, combination strategies are being explored, including the combination of immune checkpoint inhibitors with targeted therapies, radiation therapy, or other immunotherapies, aiming to enhance treatment effectiveness and address resistance observed in certain cancers.

Precision oncology

Precision medicine, a personalized approach to treatment, takes into account individual patient and tumor characteristics. Utilizing genomics, proteomics, and other omics technologies, specific genetic alterations and biomarkers are identified to guide treatment decisions. Targeted therapies and companion diagnostics are being developed to match patients with the most effective treatments for their particular cancer subtype. In the realm of precision oncology, the focus is expanding beyond common cancers with well-defined molecular alterations to include cancers harboring unique genetic mutations or alterations. With advancements in targeted therapies, such as KRAS inhibitors and antibody-drug conjugates, the treatment landscape for patients can be significantly impacted and diversified.

Liquid biopsy and minimal residual disease detection

Liquid biopsies have emerged as non-invasive tests that analyze tumor-derived materials from blood samples, offering a minimally invasive alternative to traditional tissue biopsies. These tests provide real-time information about the tumor's genetic profile, treatment response, and disease progression, revolutionizing cancer diagnosis, monitoring, and treatment decision-making. Additionally, liquid biopsies hold great potential for detecting and monitoring minimal residual disease, with ongoing research focusing on refining techniques, improving sensitivity and specificity, and establishing standardized protocols. This advancement can facilitate early relapse detection and guide treatment strategies.

Artificial intelligence and machine learning

Artificial intelligence (AI) and machine learning (ML) have the potential to revolutionize cancer research and clinical practice by analyzing vast amounts of data. These technologies can examine genomic data, medical images, electronic health records, and scientific literature to identify patterns, predict treatment responses, and develop personalized treatment plans. AI contributes to early cancer detection, pathology analysis, treatment optimization, and drug discovery. As AI and ML continue to advance, future research aims to develop more sophisticated algorithms for predictive modeling, image analysis, and pattern recognition, ultimately improving early detection, diagnosis, treatment response prediction, and outcome estimation. It is crucial to ensure the ethical and responsible implementation of AI in cancer research and clinical practice.

It is important to note that while these trends hold promise, further research and clinical trials are needed to fully evaluate their safety, efficacy, and long-term benefits. Nevertheless, they represent areas of active investigation that have the potential to revolutionize cancer research and improve patient outcomes in the near future.

In the context of the challenges faced in contemporary cancer research, how do you envision overcoming obstacles such as the translation of research findings into clinical applications?

Translating research findings into clinical applications is a complex process that involves many challenges in cancer research. Here are some angles that may help overcome these obstacles:

Collaborative efforts

Collaboration between researchers, clinicians, pharmaceutical companies, and regulatory agencies is crucial for translating research findings into clinical applications. By fostering interdisciplinary collaborations, sharing knowledge and resources, and promoting open communication, researchers can work together to bridge the gap between basic research and clinical implementation.

Preclinical studies

Robust preclinical studies are essential to validate the efficacy and safety of potential cancer therapies before moving to clinical trials. Improving the quality of preclinical research, ensuring the use of appropriate animal models that closely mimic human cancer, and conducting rigorous preclinical studies will increase the chances of successful translation to the clinic.

Clinical trial design

Designing well-designed clinical trials is crucial for evaluating the effectiveness of new therapies. It is important to consider factors such as patient selection criteria, appropriate control groups, endpoints that measure clinically meaningful outcomes, and statistical rigor. Innovative trial designs, such as adaptive and basket trials, can also facilitate the evaluation of targeted therapies in specific patient populations.

Biomarker development

Biomarkers play a vital role in guiding treatment decisions and predicting treatment responses. Investing in research to identify and validate biomarkers that can accurately predict patient outcomes and response to therapy is essential. This will enable the identification of patients who are most likely to benefit from specific treatments, leading to more targeted and personalized approaches.

Regulatory considerations

Streamlining the regulatory process is important to facilitate the translation of research findings into clinical applications. Regulatory agencies need to provide clear guidelines and accelerate the review and approval process for new therapies, especially those that demonstrate significant potential for patients with unmet medical needs.

Data sharing and standardization

Encouraging data sharing and standardization of research protocols, data formats, and analysis methods can enhance collaboration and reproducibility. Establishing comprehensive databases that integrate clinical, genomic, and treatment data can provide a valuable resource for researchers and clinicians, enabling them to make evidence-based decisions.

Funding and industry support

Continued investment in cancer research, both from the public and private sectors, is crucial for overcoming the challenges of translating research findings into clinical applications. Adequate funding and support from pharmaceutical companies can help accelerate the development and commercialization of promising therapies.

Patient engagement

Involving patients and advocacy groups in the research process can help ensure that research findings align with patient needs and preferences. Patient engagement can provide valuable insights into the design of clinical trials, the development of patient-reported outcome measures, and the implementation of interventions that address the practical challenges faced by patients.

In the long run, we envision the translation of research findings into clinical applications, leading to improved patient outcomes and advancements in cancer treatment and care.

Looking ahead, what specific research areas or questions do you plan to explore in the next five years, and how do you anticipate your work contributing to the broader landscape of cancer research and treatment?

Apart from the current hot topics mentioned above, here are some potential future research directions that may be explored in the coming years:

Genome editing

Genome editing holds immense potential in the field of cancer research and application. Techniques like CRISPR-Cas9 have revolutionized the ability to precisely modify DNA sequences, allowing researchers to target and edit cancer-related genes. Genome editing offers opportunities to study the functional impact of specific mutations, identify potential therapeutic targets, and develop novel treatment strategies. Additionally, it enables the creation of more accurate and relevant cancer models for preclinical studies. Next-generation genome editing tools and new enzymes would further advance the technology. However, existing challenges such as off-target effects, delivery methods, and ethical considerations should be well addressed. Despite these challenges, genome editing presents a promising avenue for advancing our understanding of cancer biology and improving targeted therapies in the fight against cancer.

Drug repurposing

Drug repurposing offers a promising perspective in the application of cancer treatment. By identifying existing drugs that are already approved for other medical conditions, researchers can expedite the development process and potentially bypass the lengthy and costly stages of drug discovery. Repurposing drugs for cancer treatment allows for the exploration of new treatment options with established safety profiles and known pharmacokinetics. Additionally, it offers the potential to overcome drug resistance and enhance treatment efficacy. With the vast amount of data available from clinical trials and drug databases, repurposing efforts can be guided by comprehensive analysis and computational modeling. While challenges such as intellectual property rights and clinical trial design remain, drug repurposing holds significant potential to expand the therapeutic options available for cancer patients and accelerate the delivery of effective treatments to the clinic.

Molecular classification and druggable targets

Molecular classification and the expansion of druggable targets have transformed the landscape of cancer application. Through advanced genomic profiling and molecular analysis, tumors can be classified into distinct subtypes based on their underlying molecular alterations. This classification enables personalized treatment approaches, as specific targets can be identified and matched with targeted therapies. Furthermore, the continuous expansion of druggable targets, including novel mutations and signaling pathways, provides opportunities for the development of innovative therapies. By identifying and targeting these specific molecular aberrations, precision medicine approaches can be employed to improve treatment outcomes and overcome drug resistance. The ongoing efforts to unravel the molecular complexity of cancer and expand the repertoire of druggable targets offer great promise in the advancement of cancer treatment strategies.

Nanotechnology

Nanotechnology offers exciting possibilities in cancer diagnosis, imaging, and treatment. Nanoparticles can be engineered to deliver drugs directly to tumors, enhancing drug efficacy while minimizing side effects. Additionally, nanoscale imaging agents can improve diagnostic accuracy and provide real-time information

during surgeries. The development of nanotechnology-based theranostics holds great potential for personalized cancer medicine.

Cancer immunogenomics

Understanding the complex interplay between the tumor genome and the immune system can provide valuable insights into cancer development, progression, and response to therapies. Future research may explore the field of cancer immunogenomics, combining genomic and immune profiling data to identify key genetic and immunological factors driving tumor-immune interactions. This knowledge can contribute to the development of novel immunotherapies and personalized treatment strategies.

Tumor microenvironment, single-cell sequencing, and spatial multi-omics

The tumor microenvironment and single-cell sequencing have emerged as crucial factors in cancer research. The tumor microenvironment consists of various non-cancerous cells, such as immune cells, fibroblasts, and blood vessels, that interact with cancer cells and influence tumor growth, invasion, and response to therapies. Understanding the dynamic interactions within the tumor microenvironment is essential for developing effective treatment strategies. Single-cell sequencing enables the analysis of individual cells within a tumor, providing detailed insights into cellular heterogeneity and identifying rare cell populations. This technology has the potential to uncover novel biomarkers, therapeutic targets, and mechanisms of resistance. On the other hand, spatial multi-omics can unravel tumor heterogeneity, identify spatial biomarkers, optimize drug development and treatment strategies. By integrating the knowledge of the tumor microenvironment with single-cell sequencing data and spatial multi-omics, researchers can unravel the complex interplay between cancer cells and their surrounding milieu, leading to improved diagnosis, prognosis, and personalized treatment approaches in cancer.

It is important to note that these research areas are based on my studies. The actual research directions and breakthroughs in the next five years may depend on maintaining the existing momentum or witnessing groundbreaking developments in the field.

Lastly, what advice would you offer to aspiring researchers, especially those who are just beginning their careers in cancer research, to navigate challenges, stay motivated, and make meaningful contributions to the field?

To aspiring researchers beginning their careers in cancer research, I would like to offer the following advice to navigate challenges, maintain motivation, and make meaningful contributions to the field:

Find your passion

Pursue research topics and questions that genuinely excite you and align with your interests. Passion for your work will keep you motivated, even when faced with challenges. Explore different areas within cancer research to discover what resonates with you the most.

Seek mentorship

Look for experienced mentors who can guide you through the early stages of your career. Mentors provide valuable insights, advice, and support. They can help you navigate challenges, provide feedback on your work, and offer guidance on career development.

Embrace curiosity and critical thinking

Be curious and ask thought-provoking questions. Develop strong critical thinking skills to analyze research findings, identify gaps in knowledge, and propose innovative approaches. Embrace a scientific mindset that values evidence-based decision-making and challenges existing paradigms.

Continuous learning

Commit to lifelong learning and stay updated with the latest research and technological advancements in cancer research. Attend conferences, workshops, and seminars to expand your knowledge and network with experts in the field. Dedicate time to reading scientific literature and engaging in discussions with colleagues to foster intellectual growth.

Collaborate and network

Collaborate with researchers from different disciplines and institutions to broaden your perspectives and enhance the impact of your work. Build a network of peers and mentors through professional societies, conferences, and research collaborations. Networking can lead to new opportunities, collaborations, and exposure to different research environments.

Embrace failure and learn from setbacks

Failure and setbacks are an inherent part of research. Embrace them as learning opportunities rather than personal setbacks. Analyze the reasons for failure, adapt your approach, and persist in pursuing your research goals. The resilience and perseverance developed through overcoming obstacles will contribute to your growth as a researcher.

Develop effective communication skills

Learn to communicate your research effectively to both scientific and non-scientific audiences. Develop skills in scientific writing, oral presentations, and data visualization. Clear communication increases the impact of your work, facilitates collaboration, and helps you bridge the gap between research and clinical practice.

I believe standing on the shoulders of the giants gives me a broader horizon and can rise to new heights. Research is a learning process that solves problems, like a marathon, which is a challenging exercise for me. After all, life is a marathon; everyone has his destination to go.

DECLARATIONS

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