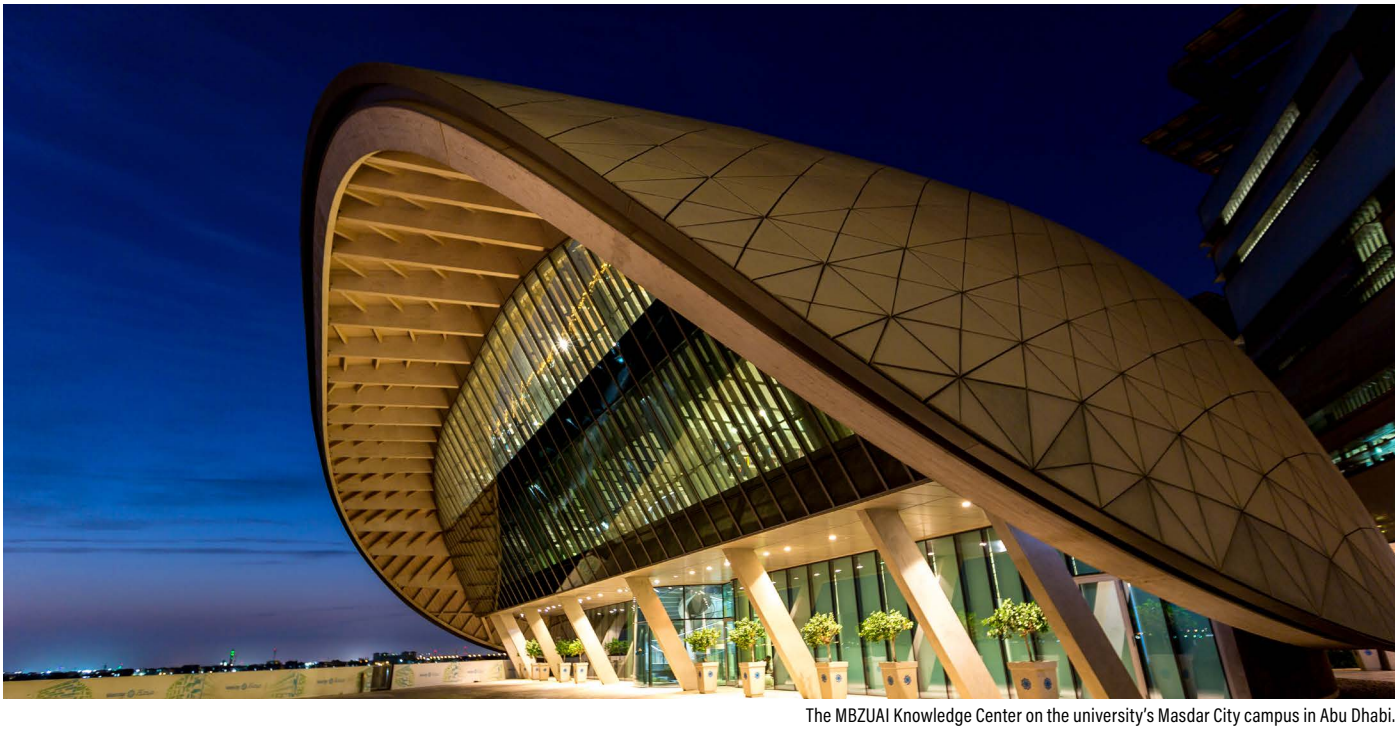

The MBZUAI Knowledge Center on the university's Masdar City campus in Abu Dhabi.

# Collaborations without borders

*Scientific collaboration is a foundational aspect of translational research, with interactions between researchers in different countries now common. Ongoing collaborations between Mohammed bin Zayed University of Artificial Intelligence (MBZUAI) and the Weizmann Institute of Science (WIS) are capitalizing on the concept of "science diplomacy" to drive progress in fields applying artificial intelligence (AI) to biomedical research.*

Within one year of its inauguration as the world's first graduate, AI-focused, research university, MBZUAI signed a memorandum of understanding with WIS to establish the MBZUAI-WIS Joint Program for AI Research. The collaboration involves not only joint research projects and training programs but also AI conferences and workshops, as well as staff and student exchange programs, that emphasize their commitment to driving AI utilization in healthcare and biomedical research.

"MBZUAI represents a tightly integrated, interdisciplinary team prepared to apply their AI expertise to any number of science-related problems," says Dr. Le Song, department chair of machine learning at MBZUAI. "MBZUAI-WIS is advancing the presence of AI in the Middle East, but its impact can be potentially societal and broadly transformative."

## Leveraging AI to drive basic and translational research

Generation of novel therapies is both time- and resource-intensive, with an extremely low success rate of drug candidates going from discovery to development. Nevertheless, the unprecedented scale of biological and clinical data generated during these activities demands methods capable of transforming these types of "big data" into clinically actionable discoveries.

Machine learning techniques have given rise to AI applications that enable clinicians and researchers to exploit large-scale, heterogeneous datasets and identify patterns connecting disease phenotype to patient physiology and characteristics. AI offers the ability to transform data into tailored, patient-specific therapeutic strategies. Three of the MBZUAI-WIS Joint Program for AI Research projects emphasize the potential impact of AI-driven, cross-disciplinary biomedical research in precision medicine.

## 1 Predicting disease onset and prognosis

In his TED talk from 2016, Eran Segal, a professor in the Department of Computer Science and Applied Mathematics at WIS, presented data illustrating the fallacy of a one-size-fits-all diet for humans. The findings demonstrated that responses to food are personal, and that a generalized approach to nutrition and diet results in wildly variable outcomes across populations. Providing personalized dietary advice required machine learning techniques to process large amounts of clinical data. The result was a model capable of not only accurately predicting a person's response to a given diet but also optimizing that diet to achieve beneficial changes in the gut microbiome.

In 2018, Dr. Segal expanded this concept into Project 10K (https://www.project10k.org.il/), a long-term observational study of 10,000 Israeli volunteers with the goal of compiling an extremely comprehensive phenotype (medical history, lifestyle, and nutritional habits) and molecular profile (including transcriptome, gut and oral microbiome, metabolome) for each individual.

Dr. Segal says they ultimately enrolled over 20,000 people, with approximately 10,000 having already undergone baseline profiling and another 2,500 completing a second round after 2 years. "We have identified novel gut bacteria with therapeutic potential for weight loss, diabetes, hypertension, and several other indications, as

PHOTO: PROVIDED BY MBZUAI

well as made discoveries related to models for biological aging," says Dr. Segal. "These findings offer opportunities to perhaps treat and improve people's health by interventions directed at reducing their biological age."

Discussions are currently underway with researchers in other countries to collect similar data in order to enhance model robustness and generalization. Dr. Segal emphasizes the importance of his MBZUAI collaborators in this process. "Drs. Le Song and Eric Xing bring novel methodologies that can handle the complex and heterogeneous nature of these extremely large datasets."

## 2 Elucidating cellular function and dynamics in native tissue

**Left to right:** Eran Segal, Nir Yosef, Le Song

Single-cell RNA sequencing allows assessment and comparison of transcriptional activity at single-cell resolution, enabling novel insights into cellular processes and their regulation and variability among cells. Understanding how transcriptomes influence and are influenced by the cell's tissue environment under different physiological states requires their analysis within intact tissue (i.e., spatial transcriptomics). Although spatial transcriptomics enables high-resolution assessment in this context, limitations exist regarding data quality. Machine learning techniques are instrumental in addressing these shortcomings to enable the generation of models that approximate tissue-specific cellular networks.

Nir Yosef, an associate professor in the Department of Systems Immunology at WIS, together with Michael I. Jordan, a laureate professor at MBZUAI, is leading a project to optimize applications of these methods to more accurately define the function of specific tissues and their disease-specific alterations. "Supplementing genome-scale cell profiling with information about tissue context can offer a better understanding of the emergence of tissue function," says Dr. Yosef. "Such realizations can be leveraged for translational applications, including identifying patient-specific therapeutic targets and stratification for medical diagnosis and treatment."

This project also involves establishment of the MBZUAI-WIS Center of AI for Spatial Transcriptomics. "We expect to become a hub for software solutions that address challenges in data analysis and the development of applications to identify spatial features capable of predicting clinical outcomes," explains Yosef.

## 3 Designing new cancer immunotherapy strategies

The tumor microenvironment (TME) comprises both cancer and immune cells that dynamically interact to determine disease status and therapeutic response, with the efficacy of cancer immunotherapy— which harnesses a patient's immune system to recognize disease-specific characteristics and thereby target care—largely dictated by patient-specific differences in this area. In the TME, the heterogeneous state of T-cells (tumor-infiltrating lymphocytes, or TILs) is particularly important from a therapeutic standpoint.

MBZUAI-WIS collaborators are targeting the TME-specific landscape of T-cell heterogeneity and dynamics using both AI and in vivo experiments to develop models capable of tracking T-cells and identifying changes in their status as functional (exhibiting antitumor activity) or dysfunctional. Given that the state of TIL populations differs between tumor type and patient, determining TME-specific changes can ultimately facilitate precision immunotherapy.

"Our aim is to perform model pretraining using public datasets to establish gene-expression patterns across different cell types and perturbations, followed by adaption of these models to supplement data from in vivo perturbations," explains MBZUAI's Song. "The pretrained model both reduces the number of necessary in vivo perturbations and increases its predictive accuracy upon inclusion of the experimental results."

This project also aims to use these models to predict optimal combination therapies to overcome cases of acquired resistance, the concept being that generation of a patient-specific TME model will allow a rapid and targeted response to resistance, as well as predict patient response.

## Driving AI innovation in biomedicine

In the press release for the joint program, leaders of both institutions emphasized the importance of empowering scientists by sharing resources and knowledge to foster a culture of international partnership and capitalize on the enormous possibilities of AI in scientific research.

"Given the broad applications of AI across disciplines, a focused understanding of traditional computational approaches is no longer sufficient for young researchers to facilitate interdisciplinary research," notes Song. "AI research now requires an integrated and collaborative approach to addressing problems across all areas of science."

Segal also emphasizes the mutually beneficial aspects of the MBZUAI-WIS partnership. "We are very excited to join forces with world-leading AI expert researchers at MBZUAI, and I believe in the power of such collaborations."



PHOTO: PROVIDED BY MBZUAI