



March 28, 2017

To Whom It May Concern,

I am writing to recommend the superior work of Dr. Shicheng Guo, an esteemed scholar in the field of clinical epigenetics. Dr. Guo is currently conducting research as a Postdoctoral Fellow at the University of California, San Diego. He has previously held positions at the University of Texas Health Science Center, the CAS-MPG (Chinese Academy of Sciences and German Max Planck Society) Partner Institute for Computational Biology, and the Institute of Rheumatology, Immunology, and Allergy in Shanghai, China. Dr. Guo received his Ph.D. in Genetics from Fudan University. As this record shows, leading institutions have repeatedly recognized Dr. Guo's excellence and have thus selected him for key research positions. This establishes Dr. Guo's position as a researcher at the top of his field. I am not personally acquainted with Dr. Guo, but I have cited his papers several times in my work, gaining new insights through his expertise. Thus, I can confirm the importance of his work to other scholars in the field, who depend on his research and publications to gain information and models for their own projects.

Please allow me to introduce myself to validate this reference. My name is Dr. Manel Esteller, and I am the Director of the Cancer Epigenetics and Biology Program (PEBC) of the Bellvitge Institute for Biomedical Research (IDIBELL). I am also a Professor of Genetics and Leader of the Cancer Epigenetics Group in the University of Barcelona School of Medicine and a Research Professor at the Catalan Institute for Research and Advanced Studies (ICREA). I hold a Ph.D. from the University of Barcelona and completed my postdoctoral research at Johns Hopkins University School of Medicine. I have also held research positions at the School of Biological and Medical Sciences at the University of St. Andrews and CNIO Cancer Epigenetics Laboratory. During my career, I have studied DNA methylation and its relationship to cancer in humans. I am currently focused the study of epigenetic machinery and mechanisms. As part of my research into current advances in the study of DNA methylation in cancer epigenetics, I have cited Dr. Guo's work in review articles for *Nature Medicine*, *Nature Reviews Genetics*, and *Genes & Cancer*. In these reviews, I express my excitement about Dr. Guo's method for investigating DNA methylation status of human cells using whole-genome bisulfite sequencing. As I describe in my citation of his research, Dr. Guo's work enables the next generation of epigenomic innovation. Having highlighted Dr. Guo's findings in my own publications, I can personally attest to the singular value and significance of his work to the field as a whole.

Dr. Guo has provided essential leadership in the area of clinical epigenetics in a series of studies on DNA methylation. In his first study, Dr. Guo and colleagues built the first human DNA methylome of human peripheral blood mononuclear cells (PBMC). To do this, he used a next-generation sequencing technique in a single base resolution, achieving both high coverage and depth. Dr. Guo's results showed that the majority of CpG sites in the human genomes are methylated. As part of this study, Dr. Guo provided methylation profiles for human genome features, including the gene promoter and gene body. He identified several features of the human genome concerning methylation, including co-methylation, haploid differentially methylated regions (hDMRs), and interaction between DNA methylome and the human DNA sequence. His study is thus a comprehensive resource for epigenomic research.

Following this paradigmatic study, Dr. Guo has continued his research into DNA methylation, focusing particularly on identifying epigenetic biomarkers. In one study published in *Clinical Epigenetics*, Dr. Guo quantitatively evaluated the diagnostic performance of adenomatous polyposis coli (APC) promoter

methylation to non-small cell lung cancer (NSCLC). To do this, Dr. Guo built a computational model that integrated DNA methylation microarray data and other genome-wide DNA methylation dataset from previous published studies. In his test, he identified a significant association between APC promoter hypomethylation and NSCLC. Based on these results, Dr. Guo concluded that an APC methylation test is an effective method for clinically diagnosing lung adenocarcinoma. Because finding biomarkers is vital to early detection and diagnosis of carcinogenesis, Dr. Guo's computational method and findings are significant contributions to the study and treatment of cancer.

Including the articles based on this research, Dr. Guo has published an astonishing 38 articles to date. Even more impressive, many of Dr. Guo's articles appear in some of the most well-respected and selective journals in the field. Dr. Guo's prolific rate of publication is indicative of a researcher at the center of major developments in the field, whose expertise is highly sought by his peers. Indeed, Dr. Guo's articles have received more than 800 citations, which shows his enormous influence on his colleagues and the direction of the field. Dr. Guo's work has also been featured in a number of widely read news sources, including Science Daily, BioPortfolio, and others, demonstrating the broad attention and interest his work has garnered across the scientific community.

Researchers have been quick to implement many of Dr. Guo's innovative discoveries in their own research. Dr. Guo's work on PBMC has been cited over 200 times, including by Hansen et al. in *Nature Genetics*, who utilized Dr. Guo's discoveries to make further conclusions about the role of hypomethylation in cancer. Landan et. al drew on Dr. Guo's high-resolution profiles of methylation patterns for their study of "Epigenetic polymorphism and the stochastic formation of differentially methylated regions in normal and cancerous tissues." As these examples demonstrate, Dr. Guo's comprehensive and thorough research on the DNA methylome has provided subsequent researchers with ample insights and inspiration for further study. Researchers from the First Affiliated Hospital of Nanjing Medical University cited Dr. Guo's study of APC methylation in NSCLC in their development of real-time monitoring for therapeutic outcomes of advanced lung cancer. Dr. Guo's research is therefore immediately applicable to medical advances that help improve the lives of cancer patients.

Finally, cancer is a devastating disease that affects millions of people in the United States. In 2016, an estimated 1,685,210 new cases of cancer were diagnosed in the U.S., with 595,690 people dying from the disease. Dr. Guo's ground-breaking research on DNA methylation provides researchers with the latest scientific understanding and diagnostic tools needed to decrease these numbers, saving thousands of lives. He is an integral part of the U.S. scientific community, and a valuable investment for the U.S. healthcare system.

Yours sincerely,



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