Preface

Although the first indication of the presence of DNA in blood occurred some 65 years ago, it was not until the early 1970s that there was a return to researching the DNA present in blood led by the pioneering studies of Maurice Stroun and Philippe Anker, in which they demonstrated the release of DNA in a controlled manner from living but not dead cells. They further showed that DNA found in the blood could be of tumor cell origin.

During the interim period, studies on the uptake and movement of DNA in cells and whole organisms gave rise to the idea that DNA could circulate within organisms—both plant and animal—and that a fraction of the DNA could be acting as a messenger. These new studies showed increases in blood DNA levels in cancer and trauma patients and were followed by measurements of increased DNA blood levels in patients suffering from sepsis, stroke, and acute myocardial infarction by the early 2000s. Clearly, the increased amounts of DNA found in cancer patients could not be used to identify the type of cancer present, and current studies are ongoing to identify suitable early markers for cancer-specific forms based on assays for individual sequences of cell-free DNA, mRNA and microRNAs with some successful early markers already available ranging from individual markers to panels of markers.

A major development involves the use of minimally invasive methods for identifying fetal cell-free DNA in the maternal blood, so leading to first-trimester identification of fetal sex and Rh status. The former has been incorporated in routine clinical practice in a number of countries as well as by direct-to-consumer testing. The development of techniques, including digital PCR and massively parallel sequencing, has allowed the detection of allelic imbalances and the precise quantification of sequences in the maternal plasma. In turn, this has enabled the deduction of maternally inherited fetal monogenic diseases as well as the accurate detection of fetal chromosomal aneuploidies such as Down syndrome in the first trimester. In addition, the determination of the fetal genome *in utero* through the sequencing of the fetal cell-free DNA in maternal blood has been achieved. Moreover, the sequencing of fetal cell-free RNAs found in amniotic fluid has opened up the possibility of identifying markers for fetal development and hence

potential developmental problems. This offers the possibility of initiating treatment either *in utero* or immediately after birth.

Thus, the study of circulating nucleic acids in plasma and serum (CNAPS) has yielded the first concrete steps as an additional arm to the other "liquid biopsy" methods already involved in predictive, preventive and personalized medicine (PPPM). More recently, the research has been extended to include studies on cell-free DNA and RNAs in other body fluids including saliva, urine, amniotic fluid, cerebrospinal fluid, bronchial lavages/aspirates, breast milk, colostrum, tears, seminal fluid and stools.

The study of circulating nucleic acids (CNA) is already playing an important role in PPPM, including the exploitation of early nucleic acid markers for (i) monitoring serial blood biomarker concentrations to screen patient groups at risk of developing a disease, (ii) estimating the severity (and staging) of a diagnosed disease, (iii) the stratification of patients with a diagnosis for a particular therapy, (iv) monitoring the response to local or systemic therapies and (v) the early detection of disease recurrence following completion of primary therapy.

As with other approaches, CNA has a crucial role to play in the integrative approach of PPPM, which is acknowledged as a priority by the WHO, UN General Assembly, and the European Union, among others. The European Association for Predictive, Preventive and Personalised Medicine (EPMA) (http://www.epmanet.eu) is at the forefront of PPPM-related initiatives and has provided an excellent scientific research platform through *The EPMA Journal* (BioMed Central, London). The EPMA organization of the *World Congress on PPPM* in Bonn, Germany on September 15-18, 2011 hosted participants from 44 countries worldwide, an event leading to the EPMA J publication of the ***General Report and Recommendations in PPPM 2012: White Paper of EPMA***. The subsequent release of the EPMA Book Series *Advances in PPPM* published by *Springer* has yielded a range of PPPM-related volumes. The current volume, *Circulating nucleic acids in early diagnosis, prognosis, and treatment monitoring: an introduction,* concerns the preparation of cell-free nucleic acids from peripheral blood and other body fluids, the analytical methods employed, and the application of these methods in PPPM. The book presents the current situation and is intended primarily for all researchers who would want to enter the field, be they PhD students, postdoctoral workers, current researchers, or clinicians. My special thanks go to the chapter authors for their contributions and the publisher for support during the preparation of this book.

London, UK Peter B. Gahan

http://www.springer.com/978-94-017-9167-0

Circulating Nucleic Acids in Early Diagnosis, Prognosis and Treatment Monitoring
An Introduction
Gahan, P.B. (Ed.)
2015, XIX, 471 p. 59 illus., 39 illus. in color., Hardcover
ISBN: 978-94-017-9167-0