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PREFACE

In some respects, the organization and fundamental concept of this symposium on extrachromosomal DNA resembles the circular nature of some of the extrachromosomal elements themselves. It is difficult to separate the beginning from the end. The symposium was organized on the premise that the diversity and complexity of primitive mitochondrial and perhaps chloroplast DNA structure and replication had more in common with many viral systems than with either prokaryotic or eukaryotic systems. This is especially striking in the case of so-called split genes. Intervening sequences in DNA were first discovered in the small DNA viruses and later in nuclear genes. But it is in yeast mitochondrial DNA that the extent of their involvement in RNA processing is most noteworthy. As reported at this symposium, it is possible to isolate mutants in some intervening sequences and analyze their effect in loci of known genetic function. Not only will such analyses in yeast mitochondrial split genes lead to a basic understanding of intervening sequences in general, but their very presence will have to be dealt with in evaluating theories on mitochondrial evolution.

It should not be surprising that the most active area of research represented at this meeting is the biogenesis of yeast mitochondria. At the close of the symposium, Pyotr Slonimski presented a brief overview that put the meeting in historical perspective. Much to the surprise of the organizers, Slonimski pointed out that the timing coincided almost to the month with the 30th anniversary of Boris Ephrussi's announcement on the petite mutation (Ephrussi, B., Hottinguer, H., and Tavlitzki, *J. Ann. Inst. Pasteur* 76, 351, April 1949). In a series of seven articles, Ephrussi and his collaborators reported on many aspects of the petite mutation with only passing reference to DNA. Since this was some 14 years before the first demonstration of mitochondrial DNA, this was certainly not a startling omission. The ensuing years have shown that yeast mitochondria have occupied a signal position in elucidating the function of extrachromosomal DNA. As we shall see, the analysis of intervening genes is especially important in yeast mitochondria, as well as the sequencing of a variety of genes of known function.

This symposium witnessed the gathering of seemingly disparate groups of researchers involved in mitochondrial, chloroplast, plasmid, and viral DNA function and replication. As will be apparent, however, great similarities exist in these systems at both the molecular and phenomenological levels. In future years, these similarities may well lead to a more basic understanding of organelle evolution and biogenesis.

I want to thank my coorganizers Piet Borst, Igor Dawid, and Sherman Weissman for their enthusiasm and assistance in organizing this symposium. We also wish to thank the Life Sciences Division of ICN Pharmaceuticals, Inc., for their continued support of the ICN–UCLA Symposia series and the National Institutes of Health for contract #263-MD-912641 (jointly sponsored by the Fogarty International Center, National Cancer Institute and National Institute for Allergy and Infectious Diseases).

CONTENTS

IX. BIOLOGICAL AND STRUCTURAL FEATURES OF KINETOPLAST AND *PODOSPORA* MITOCHONDRIAL DNA

EXTRANUCLEAR GENETICS

G.H. Beale[1]

ABSTRACT A brief survey of the development of our knowledge of extranuclear genetics is presented. The material is grouped under three headings: (1) DNA-containing cell organelles; (2) endosymbionts, and (3) virus-like particles. The extremely uneven development of research on the different examples is pointed out. Comparisons between examples in the different groups are made regarding their DNA, the presence of histone-like proteins, and the relative control of extranuclear structures by nuclear and extranuclear genes. An attempt is made to establish homologies between members of different groups, and some evolutionary hypotheses are considered. It is suggested that use of the terms "prokaryote" and "eukaryote" may be inappropriate for extranuclear DNA and should be applied to whole cells or organisms. It is also pointed out that even the meaning of the word "extranuclear" has some obscurity. The need for research on a wider range of materials than have been studied hitherto is stressed.

INTRODUCTION

Extranuclear genetics is now such a large and diversified subject that it is well-nigh impossible to write a coherent account in the short space of a single contribution to a symposium. Nevertheless there are good reasons for making the attempt: it offers an opportunity to allow one's mind to roam over the whole field before concentrating on the minutia of particular examples. It shows that though a great deal has been learnt about certain parts of the subject, others have been seriously neglected. We know far more about mitochondria than about other extranuclear structures with genetic properties, except possibly some viruses, and amongst mitochondria, most of our information comes from one organism - Saccharomyces cerevisiae.

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To illustrate the variability of mitochondria amongst different organisms, the following facts should be noted. The DNA of yeast mitochondria is in the form of a circle of about 25 μm in circumference, while in other organisms the size may vary from 5 μm to 35 μm or more. In protozoa the mitochondrial DNA may be circular, linear or (in kinetoplasts) catenated (1). The mitochondrial ribosomes of different organisms also vary a great deal in size (from 55S in animals to 80S in plants or ciliates), and there are important differences in the genes (nuclear and mitochondrial) coding for the mitochondrial ribosomal proteins in yeast, Neurospora and Paramecium (2). Thus even within the one category of mitochondria a misleading impression is created if all conclusions are based on yeast, and still greater disparity is evident when one takes into consideration cytoplasmic structures other than mitochondria.

By contrast with this diversity of extranuclear genetic systems, the classical chromosomal mechanism controlling Mendelian heredity is remarkably uniform over the whole range of eukaryotic organisms, from protista to mammals, and there we were not led far astray by basing the whole theory on Drosophila, more or less. My aim therefore in presenting this paper is to draw attention to the diversity of extranuclear phenomena, and to the necessity of studying a wider range of materials.

To illustrate the development of our knowledge of extranuclear genetics, it is interesting to compare our present programme with the proceedings of a symposium held in Paris in 1948 (3). The earlier meeting was organised by André Lwoff and entitled "Unités biologiques douées de continuité génétique". At that meeting Ephrussi presented his first results on the "petite colonie" mutants of yeast, and tentatively ascribed their determination to a cytoplasmic, non-genic, factor. L'Héritier described his CO_2-sensitive strains of Drosophila, and showed them to be controlled by cytoplasmic elements which were called at that time "génoïdes". Rhoades discussed the plastids, which had long been known to show non-Mendelian properties - ever since the observations of Correns and Baur in 1909-, though in 1948 there was still a lot of argument about whether the non-Mendelian determinants were actually inside the chloroplasts, or somewhere else in the cytoplasm, or possibly comprised some ill-defined entity known as the "plasmon".

In the discussion of these and other non-Mendelian phenomena the word "plasmagene" was used by several speakers at the Paris meeting, as a kind of alternative to real chromosomal genes. Some participants speculated that there might be a whole range of sub-cellular particles, including