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KERATINS AND KERATINIZATION:
A STRUCTURAL AND BIOCHEMICAL STUDY OF KERATINS,
RELATED PROTEINS AND THE TISSUES
THAT PRODUCE THEM.

by

George Ernest Rogers

M.Sc. (Melbourne)

Ph.D. (Cantab).

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PREFACE

A total of 83 published works including one book are noted in this thesis. Of these, the 68 papers concerned with the theme of the thesis are represented here together with 5 miscellaneous papers. Certain other papers (70, 71, 73, 76, 77), the book (69) and 4 papers currently in press are presented by title only. The thesis papers have been grouped into four separate parts (Parts I - IV) which represent fairly well the individual but related areas of my research interests. They are,

- Part I Structural Studies of α -keratin
 (27 Papers).
- Part II Protein Synthesis and Keratinization
 in the Hair Follicle (15 Papers).
- Part III The Occurrence and Origin of Citrulline
 in a Hair Protein and the Chemistry
 of Trichohyalin (14 Papers).
- Part IV Cytodifferentiation in Keratinizing
 Tissues: The Developing Down Feather
 of the Embryonic Chick as a System for
 the Study of the Expression and Structure
 of Eukaryotic Genes (12 Papers).

A complete and detailed list of these papers, the book and miscellaneous works are given below. Later,

each part is treated separately and the significance of individual papers is discussed.

The studies on the physical structure of keratins (Part I) began when I held the position of Research Officer and later Senior Research Officer in the Division of Protein Chemistry, Wool Research Laboratories of the Commonwealth Scientific and Industrial Research Organization during the years 1951 - 1954 and 1957 - 1962. At that time I carried out joint researches with colleagues R.D.B. Fraser and T.P. MacRae. Fraser and I began using light microscopy to study wool structure but it was realised that the relatively new techniques of biological electron microscopy were required, together with X-ray diffraction. I went to Cambridge to learn these techniques during the period 1954 to 1956. Later, with Fraser and MacRae on the X-ray side and myself doing electron microscopy both joint and separate works were published. Later still, B.K. Filshie joined me as a junior collaborator and he participated in publication. Although I had started some work on the biochemistry of the hair follicle during my period at C.S.I.R.O., and publications arising from this work appear in Parts II and III, these aspects did not proliferate until I took up a Readership in the Biochemistry Department of the University of Adelaide. Here, the opportunities were manifested for a multidisciplinary approach to the questions of the underlying molecular mechanisms of

keratinization, which were now my prevailing interest. Since 1963 it has been possible to build on the earlier structural and biochemical studies in collaboration with a number of research students two of whom (H.W.J. Harding and D.J. Kemp) became postdoctoral fellows (1972 - 74) and gave to the respective fields (citrulline and trichohyalin, Part III; cytodifferentiation in embryonic feather, Part IV) a great stimulus and from whence many joint publications arose with other research students and with Miss P.Y. Dyer, Senior Technician (electron microscope).

The book "Keratins" written in collaboration with Dr. R.D.B. Fraser and T.P. MacRae arose out of an invitation to Dr. Fraser by the publishers to produce a monograph that would up-date the reviewed knowledge of keratins already in the literature. Dr. Fraser invited MacRae and me to participate.

The papers given under "Miscellaneous Works" arose from my earliest research interests (Papers 71 and 72) and electron microscope studies of the morphology of skin (Papers 73, 76 and 77). The studies given in Papers 74, 75, 78 and 79 originated from the interests of various colleagues and were not my own. Nevertheless I took a significant part in the collection and collation of the data.

I give below a summary of what I believe to be the most important findings made during the course of the work presented here and represent my main contributions to science.

1. Development of methods for the application of light and electron microscopy to the study of keratinized structures.
2. The visualization of the microfibrillar structure of keratins and the overall structure of wool and hair and feather keratin.
3. Ultrastructure of the wool and hair follicle.
 - (a) structure of the glassy layer,
 - (b) the fibril-centred hypothesis of keratin synthesis.
4. The discovery of citrulline and the isopeptide link in proteins of the medulla of the hair and of the inner root sheath.
5. Explanation of the function of trichohyalin and discovery of an enzyme activity in the hair follicle that converts protein-bound arginine of trichohyalin to citrulline residues.
6. The development of cell-free systems from hair follicle homogenates that will synthesize de novo.

7. Characterisation of feather keratins as a family of homologous proteins.
8. Analysis of biochemical events during development of the embryonic feather.
Isolation and characterisation of feather keratin messenger-RNA.