1

Introduction

The endeavour to write a textbook on the *Structure and Function of Human Blood Plasma Proteins* bears an inherent risk regarding the selection of the proteins to be discussed, because this selection will always be ambiguous depending on the applied definition of the term *blood plasma protein*. Based on the classification proposed in the 1970s by Frank W. Putnam in his famous book series *The Plasma Proteins: Structure, Function and Genetic Control*, in 2002 N. Leigh Anderson and Norman G. Anderson elaborated on the classification of human blood plasma proteins in a publication in *Molecular and Cellular Proteomics*, 'The human plasma proteome: history, character and diagnostic prospects' (for details see Chapter 3). The classification proposed by Anderson and Anderson clearly shows that human plasma contains the most comprehensive version of the human proteome. The complexity of the 'plasma proteome' is quickly understood when all the various forms of blood plasma proteins present in plasma are considered: precursor and mature forms, splice variants, degradation products and, of course, all combinations of posttranslational modifications. Of course, the scope and the available space in this book require a rigid selection of the blood plasma proteins discussed in some detail. The selection is primarily based on the classification introduced by Anderson and Anderson and on personal considerations of the authors.

The main sources of information used in this book including the references therein were the following:

1. *Databases*
   UniProt Knowledgebase (Swiss-Prot and TrEMBL)
   PROSITE: database of protein domains, families and functional sites
   Protein Data Bank (PDB): an information portal to biological macromolecular structures
   MIM: Mendelian Inheritance in Man (at the NCBI)

2. *Books*
   Human Protein Data (Haeberli, 1998)
   Biochemical Pathways (Michel, 1998)
   Introduction to Protein Structure (Branden and Tooze, 1999)
   Biochemistry (Voet and Voet, 2004)
   Proteins: Structure and Function (Whitford, 2005)

3. *Articles*
   'The human plasma proteome' (Anderson and Anderson, 2002)
   'The human plasma proteome' (Anderson *et al.*, 2004)
   'The human serum proteome' (Pieper *et al.*, 2003)
   'Exploring the human plasma proteome' (Omenn, 2005)

This book is divided into three parts:

Part I
Blood Components
Blood Plasma Proteins

Human Blood Plasma Proteins: Structure and Function Johann Schaller, Simon Gerber, Urs Kämpfer, Sofia Lejon and Christian Trachsel

Part II
Domains, Motifs and Repeats
Protein Families
Posttranslational Modifications

Part III
Blood Coagulation and Fibrinolysis
The Complement System
The Immune System
Enzymes
Inhibitors
Lipoproteins
Hormones
Cytokines and Growth Factors
Transport and Storage
Additional Proteins

If not otherwise stated, the proteins discussed in this book are of human origin. The used protein name is the main name in Swiss-Prot and in some cases common synonyms are also given. All shown three-dimensional (3D) structures are from the Protein Data Bank (PDB). No model structures were included and the structures were either determined by X-ray diffraction or by nuclear magnetic resonance (NMR) spectroscopy. In a few cases nonhuman 3D structures are presented if the corresponding human 3D structure has not yet been determined. For enzymes the common EC classification system is given. Many domains, motifs and repeats or a certain stretch of sequence in a protein are characterised by a typical signature. In this book the signatures of the PROSITE database are used. In many cases diseases related to a certain protein are briefly mentioned and references to the disease database MIM (Mendelian Inheritance in Man) are given.

A limited number of references is given in each chapter and in the Data Sheets. Special emphasis was put on the quality of the references and the journals and their worldwide availability.

The information of each protein discussed in this book in some detail is summarised at the end of each chapter in a **Data Sheet**, where the most important data of each protein can be found at a glance. Proteins mentioned in the text but not discussed are compiled in the Appendix (Table A.1, human and Table A.2, nonhuman, with the corresponding reference to the database entry).

Each Data Sheet is divided into four sections:

Fact Sheet
Description
Structure
Biological Function

Table 1.1 Useful universal resource locators (URL).

URL	Description
www.expasy.org	ExPASy (Expert Protein Analysis System): proteomics server of the Swiss Institute of Bioinformatics (SIB) dedicated to protein analysis Databases: UniProt (SwissProt + TrEMBL), PROSITE, SWISS-MODEL Proteomics and Sequence Analysis Tools
pir.georgetown.edu	PIR (Protein Information Resource): integrated protein information resource for genomic and proteomic research Databases: PIRSF, iProClass, iProLink
www.rcsb.org/pdb	RCSB (Research Collaboratory of Structural Bioinformatics): information portal to biological macromolecular structures Database: PDB
www.ncbi.nlm.nih.gov	NCBI (National Center for Biotechnology Information): national resource for molecular biology information, USA
www.ebi.ac.uk	EBI (European Bioinformatics Institute): freely available data and bioinformatic services

The Fact Sheet contains the following data:

Classification:	Swiss-Prot
Abbreviations:	Most common
Structures/motifs:	Swiss-Prot and PROSITE
DB/PDB entries:	Swiss-Prot/Protein Data Bank
MW/length:	Mature Protein (without PTMs)
Concentration:	Approximate or range (if available), adult
Half-life:	Approximate or range (if available)
PTMs:	Swiss-Prot (most common)
References:	Key reference(s) on sequence and 3D structure

In the section Description each protein is briefly described (usually by only one sentence).

In the section Structure the main structural features of a protein are briefly summarised and, if available, a short description of the 3D structure is given. If available, a figure of the 3D structure is included.

Finally, in the section Biological Function the main, usually physiological, functions are briefly summarised.

A limited number of useful universal resource locators (URLs) containing reliable protein data from curated and annotated databases are tabulated in Table 1.1.

REFERENCES

Anderson and Anderson, 2002, The human plasma proteome, history, character and diagnostic prospects, *Mol. Cell. Proteomics*, **1**, 845–867.

Anderson *et al.,* 2004, The human plasma proteome. A nonredundant list developed by combination of four separate sources, *Mol. Cell. Proteomics*, **3**, 311–326.

Branden and Tooze, 1999, *Introduction to Protein Structure*, Garland Publishing, New York.

Haeberli, 1998, *Human Protein Data: Fourth Installment*, John Wiley & Sons, Ltd, Chichester, West Sussex.

Michel, 1998, *Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology*, Wiley–Spektrun, New York.

Omenn, 2005, Exploring the human plasma proteome. The HUPO plasma proteome project (HPPP). *Proteomics*, **5** (13), 3223–3550.

Pieper *et al.*, 2003, The human serum proteome: display of nearly 3700 chromatographically separated protein spots on two-dimensional electrophoresis gels and identification of 325 distinct proteins. *Proteomics*, **3**, 1345–1364.

Putnam, 1975–1987, *The Plasma Proteins: Structure Function and Genetic control*, Academic Press, New York.

Voet and Voet, 2004, *Biochemistry*, John Wiley & Sons, Ltd, Chichester West Sussex.

Whitford, 2005, *Proteins: Structure and Function*, John Wiley & Sons, Ltd, Chichester West Sussex.