seems contrary to the long-held hypothesis that an amino acid codes for a single unique 3-D structure.[60] Amyloid plaques or protein aggregations in the brain are also associated with Alzheimer's disease and Parkinson's disease, conditions not considered prion-based but also dependent on aberrant protein folding.[61] The primary structure does not absolutely determine the tertiary folding structure. It is now widely believed that gene expression alone largely, but not exclusively, controls the protein's 3-D properties.

III. Structurally similar, sequence dissimilar proteins

With the discovery of increasingly more protein structures, it has further become evident that many proteins that possess similar structures share only a very small number of identical residues in structurally associated positions.[62] Various structurally similar protein pairs have only a minimal amount of sequence identity. This suggests that many sequence positions do not play a significant role in structure determination, and folding determinants are restricted to a limited number of sequence residues.[63] Structurally similar proteins do therefore not necessarily reflect sequence-similar proteins.[64] Some proteins bearing diverse sequences with essentially no sequence homology, do fold into the same structure. With the protein's effect depending on the structure, large numbers of different proteins are able to perform the same functions.[65]

IV. Posttranslational modifications (PTM)

An important component of protein regulation and function is the modification of protein structures, which occur either co- or posttranslationally. Translation refers to

60 Tatzelt, Jorg/Winklhofer, Konstanze F., Folding and Misfolding of the Prion Protein in the Secretory Pathway, 11 Amyloid 2004, 162, 166.

61 Tatzelt, Jorg/Winklhofer, Konstanze F., Folding and Misfolding of the Prion Protein in the Secretory Pathway, 11 Amyloid 2004, 162, 162.

62 Jaenichen, Hans-Rainer/Mcdonell, Leslie A./Haley, James F., Jr., From Clones to Claims, Cologne, Berlin, Bonn, Munich 2002, 167; molecular biologists thus attempted to identify the common hidden information within these sequences that directs them to assume similar folds.

63 Kleist, Peter, Biomarker und Surrogat-Endpunkte: Garanten für eine schnellere Zulassung von neuen Arzneimitteln?, 83 Schweizerische Ärztezeitung 2022, 2347, 2350.

64 Wachenfeld, Joachim, The Patenting of Protein Structures, http://www.vossiusandpartner.com/eng/publication/mip-yearbook.html 2002.

65 Structural protein families are also called 'protein superfamilies'; see: Hultquist, Steven J./Robert Harrison, and Yongzhi Yang, Patenting Bioinformatic Inventions: Emerging Trends in the United States, 20 Nature Biotechnology 2002, 743; 771. A list of protein superfamilies with structure-based-sequence-alignment is available at: http://www-cryst.bioc.cam.ac.uk/~campass/superfamily.html, last checked on May 06, 2005.

the process in which the genetic code carried by mRNA directs the synthesis of proteins from amino acids.[66] Through constant modification of the protein, organisms accommodate radically different protein expression in different parts of the body and in different stages of the life cycle. Although amino acids can be predicted from nucleotide sequences, posttranslational modifications to proteins, in general, cannot.

Once synthesized on the ribosomes, proteins are subject to a multitude of modification steps. Because they are cleaved (thus eliminating signal sequences, transit or pro-peptides and initiator methionines), many simple chemical groups (for example acetyl, methyl, phosphoryl) as well as more complex molecules (such as sugars and lipids) can associate with them. Moreover, they can be internally or externally cross-linked (example: disulfide bonds). So far, over 200 different modifications have been described. The complexity due to all these modifications is compounded by the high level of diversity that alternative splicing[67] can produce at the level of the sequence. Many PTM have well described roles in signal transduction and the regulation of cellular processes. In contrast, other modifications are much less well documented but are also likely to play very important roles within the cell. Identifying the type and location of these proteins is a first step in understanding their regulatory potential. The complex study of posttranslational modifications is one major objective of proteomics and is referred to as 'PTM proteomics'. [68]

V. Role of Enzymes and their chemical activity

One important function performed by proteins is the ability to catalyze chemical reactions.[69] The biological catalysts were named enzymes.[70] Enzymes are usually specific to the reaction they catalyze and the chemical substances involved in the reaction. Many enzymes are composed of several proteins acting together as a unit.

66 Human Genome Project Information, Glossary of the Human Genome Project, available at http://www.ornl.gov/TechResources/Human_Genome/glossary/. Recent advances in mimicking PTMs are helping to elucidate the role of the modifications and are the subject of high expectations for future pharmaceuticals, Davis, Benjamin G., Mimicking Posttranslational Modifications of Proteins, 303 Science 2004, 480.

67 Alternative splicing of mRNA permits that many gene products with different functions are produced from a single coding sequence, see Brett, David/Pospisil, Heike et al., Alternative splicing and genome complexity, Nature Genetics 30, 2 (2001).

68 MacCoss, Michael J./Hayes McDonald; Saraf,/Saraf, Anita/Sadygov, Rovshan/Clark, Judy M./Tasto, Joseph J./Gould, Kathleen L./Wolters, Dirk/Washburn, Michael/Weiss, Avery/Clark, John I./Yates, John R., Shotgun Identification of Protein Modifications from Protein Complexes and Lens Tissue, 99 Proceedings of the National Academy of Science of the United States of America 2002, 7900, 7901.

69 Catalytic function was amongst the first biological roles recoginzed in proteins through the work of Eduard Buchner and Emil Fischer., Whitford, David, Proteins: Structure and Function, Chichester, West Sussex, U.K., 2005, 189.

70 The name derived from the Greek for 'in yeast' - 'en' 'zyme', Whitford, David, Proteins: Structure and Function, Chichester, West Sussex, U.K., 2005, 189.