2016

# Classifying Lipoproteins Based on Their Polar Profiles.

Carlos Polanco
*Universidad Nacional Autónoma de México*

Jorge Alberto Castañón-González
*Universidad Autónoma del Estado de Morelos*

Thomas Buhse
*Universidad Autónoma del Estado de Morelos*

Vladimir N. Uversky
*University of South Florida*, vuversky@usf.edu

Rafael Zonana Amkie
*Universidad Anahuac*

ACTA ABP BIOCHIMICA POLONICA

Vol. 63, No 2/2016
235–241
http://dx.doi.org/10.18388/abp.2014_918

Regular paper

# Classifying lipoproteins based on their polar profiles

Carlos Polanco[1]✉ , Jorge Alberto Castañón-González[2], Thomas Buhse[3], Vladimir N. Uversky[4,5,6] and Rafael Zonana Amkie[7]

[1]Department of Mathematics, Faculty of Sciences, Universidad Nacional Autónoma de México, C.P. 04510 D.F., México; [2]Departments of Critical Care Medicine and Biomedical Research, Hospital Juárez de México, D.F. 07760 México; [3]Centro de Investigaciones Químicas, Universidad Autónoma del Estado de Morelos, C.P. 62209 Chamilpa, Cuernavaca, Morelos, México; [4]Department of Molecular Medicine and USF Health Byrd Alzheimer's Research Institute, Morsani College of Medicine, University of South Florida, MDC07 Tampa, FL 33647, USA; [5]Department of Biological Sciences, Faculty of Science, King Abdulaziz University, Jeddah, Saudi Arabia; [6]Institute for Biological Instrumentation, Russian Academy of Sciences, 142290 Pushchino, Moscow Region, Russia; [7]Faculty of Health Sciences, Universidad Anahuac, C.P. 52786 Huixquilucan Estado de Mexico, México

**The lipoproteins are an important group of cargo proteins known for their unique capability to transport lipids. By applying the Polarity index algorithm, which has a metric that only considers the polar profile of the linear sequences of the lipoprotein group, we obtained an analytical and structural differentiation of all the lipoproteins found in UniProt Database. Also, the functional groups of lipoproteins, and particularly of the set of lipoproteins relevant to atherosclerosis, were analyzed with the same method to reveal their structural preference, and the results of Polarity index analysis were verified by an alternate test, the Cumulative Distribution Function algorithm, applied to the same groups of lipoproteins.**

**Key words**: potential of association; lipoproteins; polar balance; polarity index method; unfolded proteins; folded proteins; partially folded proteins; intrinsically disordered proteins; atherosclerosis

**Received**: 15 October, 2014; revised: 30 December, 2015; accepted: 23 February, 2016; available on-line: 08 April, 2016

## INTRODUCTION

Studies conducted in the 1980s documented a direct correlation between the high blood lipid levels and atherosclerosis (Guyton & Klemp, 1989). They also demonstrated that lowering lipid levels in the blood was associated with a reduction in the cardiovascular disease-related events and atherosclerosis. Parallel studies showed that lipoproteins; i.e., special particles containing both proteins and lipids bound to proteins, represent an important form of lipids transportation in aqueous media (Kostnet, 1983; Morrisett *et al*., 1975; Scanu & Wisdom, 1972).

Lipoproteins differ in the protein to lipids ratio and, in particular, in apolipoproteins and lipids that they contain. For example, the major apolipoproteins include apoE, apoB, apoA-I, apoA-II, apoA-IV, apoC-I, apoC-II, and apoC-III (Mahley *et al*., 1984). It was also pointed out that being involved in the transport and redistribution of lipids among various cells and tissues, specific apolipoproteins contribute significantly to the regulation of lipoprotein metabolism (Mahley *et al*., 1984). Based on their density defined by the protein to lipids ratios, lipoproteins are grouped into six classes: Chylomicrons, Very Low Density Lipoproteins (VLDL), Intermediate Density Lipoproteins (IDL), Low Density Lipoproteins (LDL), High Density Lipoproteins (HDL), and lipoproteins relevant to Atherosclerosis (Atherosclerosis) (Table 1) (Garrett & Grisham, 2012; Koba *et al*., 2003).

In order to deepen the understanding of this important group of cargo-proteins specialized in the transport of lipids, we applied the supervised computational tool called Polarity index method (Polanco *et al*., 2012), which has already been used in the analysis of other groups of peptides and proteins (Polanco & Samaniego, 2009; Polanco *et al*., 2012; 2013; 2013a; 2014a; 2014b; 2014c; 2014d; 2014e). Here, this technique was used to characterize Chylomicrons, VLDLs, IDLs, LDLs, HDLs, and Atherosclerosis, i.e. large VLDL, small dense LDL, and small DHDL subclasses (Koba *et al*, 2003). Polarity index method performed effective identification of the above mentioned groups of lipoproteins based on the records of the 16 possible polar incidents chosen from the four polar groups: polar positively charged (P+), polar negatively charged (P–), polar neutral (N), and nonpolar (NP). This approach can also associate some structural features (e.g., the intrinsic disorder of the proteins) with a group of proteins. This work aims at a comprehensive analysis of the cargo-proteins, even though it is known that fragments of these proteins possess different structural profiles, and that structures of apolipoproteins can change due to the binding and release of lipids. The calibration of the polarity index method was done with the entire set of human lipoproteins (full-length proteins and their fragments, Table 1) downloaded from UniProt Database (Magrane, 2011) and split into the mentioned categories. These same proteins were checked for their structural classifications (Table 2): unfolded, partially folded, or folded based on the correlation with the corresponding protein sets from Oldfield *et al*. (Supplementary material, Oldfield *et al*., 2005). The results of polarity index method were verified with an alternate test, by applying a Cumulative Distribution Function algorithm over the same groups of lipoproteins (Dunker *et al*., 2000).

## MATERIAL AND METHODS

The latest version of the polarity index method (Polanco *et al*., 2012) is fully automated.

✉e-mail: polanco@unam.mx

**Abbreviations**: HDL, High Density Lipoproteins; IDL, Intermediate Density Lipoproteins; LDL, Low Density Lipoproteins; VLDL, Very Low Density Lipoproteins

**Table 1. Set of Lipoproteins.**

| Number | Description | Symbol | Search engine |
|---|---|---|---|
| 19 | High-density | HDL | ("high density lipoprotein" AND "homo sapiens") AND hdl AND reviewed:yes NOT "lipoprotein binding protein" NOT (disease:"high density lipoprotein") |
| 0 | Intermediate density lipoprotein | IDL | ("intermediate density lipoprotein" AND "homo sapiens") AND idl AND reviewed:yes NOT "lipoprotein binding protein" NOT (disease:"intermediate density lipoprotein") |
| 51 | Low density lipoprotein | LDL | ("low density lipoprotein" AND "homo sapiens") AND ldl AND reviewed:yes NOT "lipoprotein binding protein" NOT (disease:"low density lipoprotein") |
| 17 | Very low density lipoprotein | VLDL | ("very low density lipoprotein" AND "homo sapiens") AND vldl AND reviewed:yes NOT "lipoprotein binding protein" NOT (disease:"very low density lipoprotein") |
| 14 | Chylomicrons density lipoprotein | Chylomicrons | ("chylomicrons" AND "homo sapiens") AND chylomicrons AND reviewed:yes NOT "lipoprotein binding protein" NOT (disease:"chylomicrons density lipoprotein") |
| 15 | Lipoproteins relevant to atherosclerosis | Atherosclerosis | (lipoproteins atherosclerosis AND organism:"Homo sapiens (Human) [9606]") |

103 Extracted lipoproteins downloaded from Uniprot Database (Magrane, 2011). Considering only those present in human beings, and with the annotation "reviewed".

**Metrics.** The polarity index is a supervised type method of the Quantitative Structure Activity Relationship (QSAR), which evaluates a single physiochemical property, the Polarity. Its metric requires data training (Tables 1, 2). Each data training set consists of sequences of amino acids which were previously converted to their numerical equivalent according to the rule: {P+, P-, N, NP}: P- = {D, E}, P+ = {H, K, R}, NP = {A, F, I, L, M, P, V, W}, and N = {C, G, N, Q, S, T, Y} (Timberlake, 1992). Each pair of amino acids in the sequence is counted and registered in an incident matrix; i.e., (row, column) = (amino acid A, amino acid B). These pairs of amino acids are formed when reading the amino acid sequence of each protein from N-terminus to C-terminus (from left to right equivalently), moving one amino acid at a time. The incident matrix (from the training data) is compared with the corresponding matrix of each target sequence. Those sequences that score greater than the default percentage (Table 3), are considered to be candidate proteins.

**UniProt database preparation.** 101 lipoproteins present in *Homo sapiens* grouped in six classes were downloaded from the UniProt database (Magrane, 2011) on September 30, 2014 (Table 1). We verified that each of the protein exists in only one of the sets. This restriction removed the group of Intermediate Density Lipoprotein (IDL), so only five types of lipoproteins were studied.

**Supplementary material.** 352 fragments with known structural attributes that were properly annotated in the supplementary material (Table 2) of Oldfield *et al.* (Oldfield *et al.*, 2005) were considered.

Table 2. Set of structural proteins.

| 103 Unfolded proteins | 97 Folded proteins | 152 Partially folded proteins |
|---|---|---|

352 structural fragments extracted from supplementary material (Oldfield *et al.*, 2005).

**Test plan.** Three tests were performed to measure the two following aspects: the property of being cargoprotein, and the level of structural disorder.

The polarity index method (Polanco *et al.*, 2012) calibrated with every lipoprotein group (Table 1) in order to: (i) measure the number of hits during the identification of lipoproteins (Table 3), and (ii) plot the relative frequency of each lipoprotein group (Fig. 1).

The polarity index method calibrated with each group of ordered, disordered and partially disordered fragments (Table 2) in order to measure: (i) the correlation between the Lipoproteins groups and groups of various disorders (Table 4), and, *vice versa*, (ii) the correlation between the disorder parameters and the lipoprotein groups (Table 5).

Points 2 and 3 show that the polarity index method is a bijection; i.e., it finds correlations between Group A and Group B, and between Group B and Group A.

The Cumulative Distribution Function algorithm (Dunker *et al.*, 2000) calibrated with the disordered fragments in order to be applied on the lipoprotein groups.

## RESULTS

The polarity index method (Polanco *et al.* 2012) identified, with a high efficiency of 75%, each of the group of Lipoproteins (Table 3). It also provided means to plot the distribution of relative frequencies of each group (Fig. 1). Figure 1 illustrates that such distributions correlated well with the results in Table 3, showing that the locations of the inflection points in the x-axis do not match for the groups. Although the correlation between the lipoprotein groups with structural features (Table 4) is not definitively conclusive, because of the relatively low efficiency of 55% on the scale of 100%, this analysis suggests that all the lipoprotein groups have the folded-partially folded profile. The affinity of the structural features to the lipoprotein groups (Table 5) corroborates the aforementioned finding that these proteins are characterized by the folded-partially folded profile. The Cumulative Distribution Function analysis (see Materials & Methods, Test plan) did not reach a definitive conclusion on the structural assignment of lipoproteins.

## DISCUSSION

Since the experimental evidence (Kay *et al.*, 1982) correlates various diseases to structural characteristics of lipoproteins, our work brought in an analytical verification for the polar differentiation of the subgroups studied. These polar differences are not observable in the points of maximum and minimum (non-degenerated singularities) (Thom, 1952), but are evidenced by variability of the location of the inflection points (degenerated

**Table 3. Classification of Lipoproteins**

| Lipoproteins → Lipoproteins | HDL | LDL | VLDL | Chylomicrons | Atherosclerosis |
|---|---|---|---|---|---|
| HDL | 89 | 27 | 35 | 29 | 27 |
| LDL | 53 | 84 | 47 | 43 | 55 |
| VLDL | 21 | 20 | 82 | 36 | 36 |
| Chylomicrons | 21 | 12 | 35 | 86 | 36 |
| Atherosclerosis | 11 | 8 | 24 | 21 | 73 |

Number of hits (%) for the each pair of Lipoproteins groups (Magrane, 2011), according to polarity index method (Polanco *et al*., 2012), at the level of efficiency greater than 75%.

**Table 4. Lipoproteins *versus* Structural profiles**

| Lipoproteins → Structural | Folded | Partially folded | Unfolded |
|---|---|---|---|
| HDL | 27 | 4 | 11 |
| LDL | 59 | 8 | 23 |
| VLDL | 12 | 3 | 9 |
| Chylomicrons | 15 | 2 | 11 |
| Atherosclerosis | 13 | 0 | 4 |

Number of hits (%) for Lipoproteins (Magrane, 2011) in regards to their structural profiles (*Oldfield et al., 2005*), according to polarity index method (Polanco *et al*., 2012), at the level of efficiency equal to 100%

**Table 5. Structural profiles *versus* Lipoproteins**

| Structural → Lipoproteins | HDL | LDL | VLDL | Chylomicrons | Atherosclerosis |
|---|---|---|---|---|---|
| Folded | 37 | 31 | 18 | 29 | 36 |
| Partially folded | 16 | 12 | 6 | 7 | 9 |
| Unfolded | 0 | 10 | 0 | 7 | 0 |

Number of hits (%) for structural profiles (*Oldfield et al., 2005*) in regards to the Lipoproteins (Magrane, 2011), according to polarity index method (Polanco *et al*., 2012), at the level of efficiency greater than 75%.

singularities), where the locations of all of these points are not matching between different curves. The polarity index method was used to measure all these sequence-based differences and, because of this, exhibited a high level of efficiency (75–86%) in the identification of the subgroups studied. We think that the efficiency of this method was due to the comprehensive nature of its metric that considers the 16 possible polar interactions and does not assess the quality of the polarity of the protein with a single number. Such use of 16 measures and not only one provides more comprehensive evaluation of the polarity of the protein.

Although finding the degree of intrinsic disorder (Uversky, 2002) of proteins provides a useful means for protein analysis, we did not find a reliable correlation between the structural assignment of a given protein to ordered, unfolded, or partially ordered structural categories and its classification to a given lipoprotein class. There are results (Knowles *et al*., 2014; Uversky & Fink, 2004; Uversky, 2009; 2010; 2014) suggesting that the degree and/or proportion of intrinsic disorder of the proteins are associated with increased risk of amyloidosis (Pepys, 2006). The amyloidogeneity of a protein can be typically assigned to its some specific fragments (Pawlicki *et al*., 2008). However, our results only showed that the human lipoproteins possess a polarity profile typical for the folded-partially folded proteins and this correlation was rather poor (47% efficiency). We assume that these results can be explained by the relative insensitivity of the method (which assessed the degree of "disorder" for the entire protein) to the presence of local disorder in some protein fragments. Also, our method analyzed the intrinsic polarity of the polypeptide chain of the protein without considering the fact that the lipid has a polarity too, and therefore a specific weight should be added to the final profile of the cargo-protein. To appropriately address these issues, it will be necessary to measure the polarity profile of a carrier protein with and without the lipid, as well as the profile of the lipid transported.

It is pertinent to mention that the polarity index method corresponds to the parallelism scheme known as "master-slaves" (Dijkstra, 1968), so its processing time is 1/n, where "n" is the number of processors in the computer. Therefore, it is possible to use this method to analyze the entire set of proteins and protein regions of a fixed length "n". For example, if one would aim to analyze all possible protein fragments of the length of 5 amino acids, the number of such fragments would be $20^5 = 3200000$. Assuming that the processing time spent by the method to assess each protein/fragment would be 0.001s, then the time required to analyze all possible fragments would be $3200000 \times 0.001\text{s} = 3200\text{s}$. However if the computer would have 10 processors, then the processing time would be just 320s (one tenth part of the computing power on a uni-processor system). Using this approach, it is possible now to process protein fragments of the length of up to 13 amino acids, because the supercomputers are usually formed by more than 4000 processors.

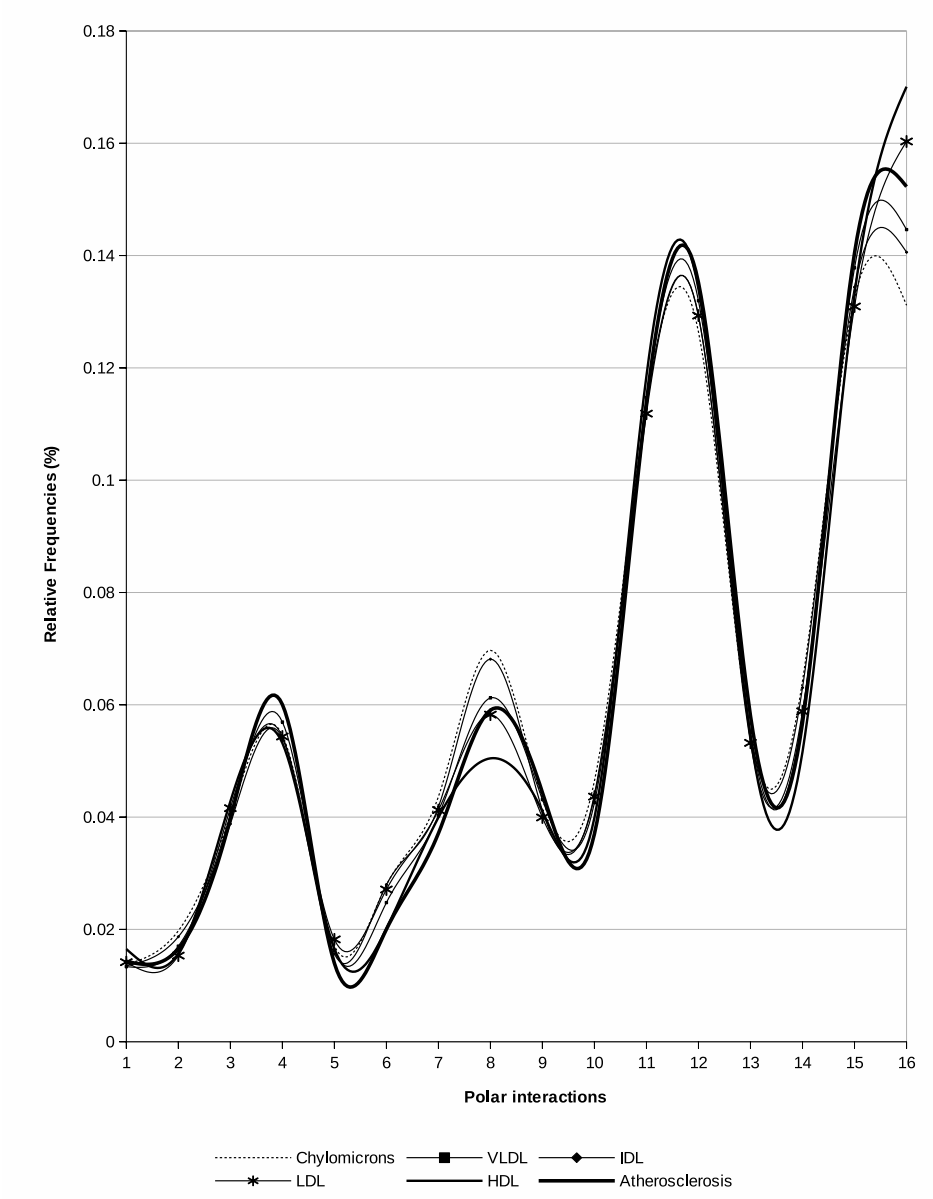


**Figure 1. Distribution of the relative frequencies of the six groups of Lipoproteins. The x-axis represents the 16 polar interactions (Materials & Methods, Metrics).**

## CONCLUSIONS

The Polarity index method is an effective and simple algorithm that can be used as a "front-line filter" for the construction of computational tools for identification and characterization of lipoproteins, as well as for the analysis of protein regions with parallel computing.

### Availability

The test-files, and polarity index method program must be requested from the corresponding author (polanco@unam.mx).

### Conflict of Interests

We declare that we do not have any financial nor personal interest with other people or organizations that could inappropriately influence (bias) our work.

### Author Contributions

Theoretical conception and design: CP. Computational performance: CP. Data analysis: CP, TB, VU, and JACG. Tables: RZ. Results discussion: CP, TB, VU, and JACG.

### Acknowledgements

The authors want to thank Concepción Celis Juárez whose suggestions and proof-reading have greatly improved the original manuscript, and we also acknowledge the Computer Science department at Institute de Ciencias Nucleares at the Universidad Nacional Autónoma de México for support, we gratefully acknowledge financial support by the Mexican-French bilateral research grant CONACYT (188689) - ANR (12-IS07-0006).

## REFERENCES


Adachi H, Tsujimoto M, Arai H, Inoue K (1997) Expression cloning of a novel scavenger receptor from human endothelial cells. *J Biol Chem* **272**: 31217–31220.

Albertsen HM, Smith SA, Melis R, Williams B, Holik P, Stevens J, White R (1996) Sequence, genomic structure, and chromosomal assignment of human DOC-2. *Genomics* **33**: 207–213.

Anderson RA, Sando GN (1991) Cloning and expression of cDNA encoding human lysosomal acid lipase/cholesteryl ester hydrolase. Similarities to gastric and lingual lipases. *J Biol Chem* **266**: 22479–22484.

Bechtel S, Rosenfelder H, Duda A, Schmidt CP, Ernst U, Wellenreuther R, Mehrle A, Schuster C, Bahr A, Blöcker H, Heubner D, Hoerlein A, Michel G, Wedler H, Köhrer K, Ottenwälder B, Poustka A, Wiemann S, Schupp I (2007) The full-ORF clone resource of the German cDNA Consortium. *BMC Genomics* **8**: 399–399.

Garrett RH, Grisham CM (2012) *Biochemistry* 5 edn, pp 1288. ISBN-13: 978-1133106296.

Brown ML, Ramprasad MP, Umeda PK, Tanaka A, Kobayashi Y, Watanabe T, Shimoyamada H, Kuo WL, Li R, Song R, Bradley WA, Gianturco SH (2000) A macrophage receptor for apolipoprotein B48: cloning, expression, and atherosclerosis. *Proc Natl Acad Sci USA* **97**: 7488–7493.

Brown SD, Twells RC, Hey PJ, Cox RD, Levy ER, Soderman AR, Metzker ML, Caskey CT, Todd JA, Hess JF (1998) Isolation and characterization of LRP6, a novel member of the low density lipoprotein receptor gene family. *Biochem Biophys Res Commun* **248**: 879–888.

Calvo D, Vega MA (1993) Identification, primary structure, and distribution of CLA-1, a novel member of the CD36/LIMPII gene family. *J Biol Chem* **268**: 18929–18935.

Clark HF, Gurney AL, Abaya E, Baker K, Baldwin D, Brush J, Chen J, Chow B, Chui C, Crowley C, Currell B, Deuel B, Dowd P, Eaton D, Foster J, Grimaldi C, Gu Q, Hass PE, Heldens S, Huang A, Kim HS, Klimowski L, Jin Y, Johnson S, Lee J, Lewis L, Liao D, Mark M, Robbie E, Sanchez C, Schoenfeld J, Seshagiri S, Simmons L, Singh J, Smith V, Stinson J, Vagts A, Vandlen R, Watanabe C, Wieand D, Woods K, Xie MH, Yansura D, Yi S, Yu G, Yuan J, Zhang M, Zhang Z, Goddard A, Wood WI, Godowski P, Gray A (2003) The secreted protein discovery initiative (SPDI), a large-scale effort to identify novel human secreted and transmembrane proteins: a bioinformatics assessment. *Genome Res* **13**: 2265–2270.

D'Esposito M, Ciccodicola A, Gianfrancesco F, Esposito T, Flagiello L, Mazzarella R, Schlessinger D, D'Urso M (1996) A synaptobrevin-like gene in the Xq28 pseudoautosomal region undergoes X inactivation. *Nat Genet* **13**: 227–229.

Day JR, Albers JJ, Gilbert TL, Whitmore TE, McConathy WJ, Wolfbauer G (1994) Purification and molecular cloning of human apolipoprotein F. *Biochem Biophys Res Commun* **203**: 1146–1151.

de Bruijn MH, Fey GH (1985) Human complement component C3: cDNA coding sequence and derived primary structure. *Proc Natl Acad Sci USA* **82**: 708–712.

Dijkstra EW (1968) The structure of the 'THE'-multiprogramming system, Communications of the ACM **11**: 341–346. doi:10.1145/363095.363143.

Ding K, McDonough SJ, Kullo IJ (2007) Evidence for positive selection in the C-terminal domain of the cholesterol metabolism gene PCSK9 based on phylogenetic analysis in 14 primate species. *PLoS One* **2**: E1098–E1098.

Dong Y, Lathrop W, Weaver D, Qiu Q, Cini J, Bertolini D, Chen D (1998) Molecular cloning and characterization of LR3, a novel LDL receptor family protein with mitogenic activity. *Biochem Biophys Res Commun* **251**: 784–790.

Drayna D, Jarnagin AS, McLean J, Henzel W, Kohr W, Fielding C, Lawn R (1987) Cloning and sequencing of human cholesteryl ester transfer protein cDNA. *Nature* **327**: 632–634.

Duchateau PN, Pullinger CR, Orellana RE, Kunitake ST, Naya-Vigne J, O'Connor PM, Malloy MJ, Kane JP (1997) Apolipoprotein L, a new human high density lipoprotein apolipoprotein expressed by the pancreas. Identification, cloning, characterization, and plasma distribution of apolipoprotein L. *J Biol Chem* **272**: 25576–25582.

Dunker AK, Obradovic Z, Romero P, Garner EC, Brown CJ (2000) Intrinsic protein disorder in complete genomes. *Genome Inform Ser Workshop Genome Inform* **11**: 161–171.

Fojo SS, Law SW, Brewer HB Jr (1987) The human preproapolipoprotein C-II gene. Complete nucleic acid sequence and genomic organization. *FEBS Lett* **213**: 221–226.

Fojo SS, Law SW, Brewer HB Jr (1987) The human preproapolipoprotein C-II gene. Complete nucleic acid sequence and genomic organization. *FEBS Lett* **213**: 221–226.

Gåfvels ME, Caird M, Britt D, Jackson CL, Patterson D, Strauss JF 3rd (1993) Cloning of a cDNA encoding a putative human very low density lipoprotein/apolipoprotein E receptor and assignment of the gene to chromosome 9pter-p23. *Somat Cell Mol Genet* **19**: 557–569.

Garcia CK, Wilund K, Arca M, Zuliani G, Fellin R, Maioli M, Calandra S, Bertolini S, Cossu F, Grishin N, Barnes R, Cohen JC, Hobbs HH (2001) Autosomal recessive hypercholesterolemia caused by mutations in a putative LDL receptor adaptor protein. *Science* **292**: 1394–1398.

Gerhard DS, Wagner L, Feingold EA, Shenmen CM, Grouse LH, Schuler G, Klein SL, Old S, Rasooly R, Good P, Guyer M, Peck AM, Derge JG, Lipman D, Collins FS, Jang W, Sherry S, Feolo M, Misquitta L, Lee E, Rotmistrovsky K, Greenhut SF, Schaefer CF, Buetow K, Bonner TI, Haussler D, Kent J, Kiekhaus M, Furey T, Brent M, Prange C, Schreiber K, Shapiro N, Bhat NK, Hopkins RF, Hsie F, Driscoll T, Soares MB, Casavant TL, Scheetz TE, Brownstein MJ, Usdin TB, Toshiyuki S, Carninci P, Piao Y, Dudekula DB, Ko MS, Kawakami K, Suzuki Y, Sugano S, Gruber CE, Smith MR, Simmons B, Moore T, Waterman R, Johnson SL, Ruan Y, Wei CL, Mathavan S, Gunaratne PH, Wu J, Garcia AM, Hulyk SW, Fuh E, Yuan Y, Sneed A, Kowis C, Hodgson A, Muzny DM, McPherson J, Gibbs RA, Fahey J, Helton E, Ketteman M, Madan A, Rodrigues S, Sanchez A, Whiting M, Madari A, Young AC, Wetherby KD, Granite SJ, Kwong PN, Brinkley CP, Pearson RL, Bouffard GG, Blakesly RW, Green ED, Dickson MC, Rodriguez AC, Grimwood J, Schmutz J, Myers RM, Butterfield YS, Griffith M, Griffith OL, Krzywinski MI, Liao N, Morin R, Palmquist D, Petrescu AS, Skalska U, Smailus DE, Stott JM, Schnerch A, Schein JE, Jones SJ, Holt RA, Baross A, Marra MA, Clifton S, Makowski KA, Bosak S, Malek J; MGC Project Team (2004) The status, quality, and expansion of the NIH full-length cDNA project: the Mammalian Gene Collection (MGC). *Genome Res* **14**: 2121–2127.

Gregory SG, Barlow KF, McLay KE, Kaul R, Swarbreck D, Dunham A, Scott CE, Howe KL, Woodfine K, Spencer CC, Jones MC, Gillson C, Searle S, Zhou Y, Kokocinski F, McDonald L, Evans R, Phillips K, Atkinson A, Cooper R, Jones C, Hall RE, Andrews TD, Lloyd C, Ainscough R, Almeida JP, Ambrose KD, Anderson F, Andrew RW, Ashwell RI, Aubin K, Babbage AK, Bagguley CL, Bailey J, Beasley H, Bethel G, Bird CP, Bray-Allen S, Brown JY, Brown AJ, Buckley D, Burton J, Bye J, Carder C, Chapman JC, Clark SY, Clarke G, Clee C, Cobley V, Collier RE, Corby N, Coville GJ, Davies J, Deadman R, Dunn M, Earthrowl M, Ellington AG, Errington H, Frankish A, Frankland J, French L, Garner P, Garnett J, Gay L, Ghori MR, Gibson R, Gilby LM, Gillett W, Glithero RJ, Grafham DV, Griffiths C, Griffiths-Jones S, Grocock R, Hammond S, Harrison ES, Hart E, Haugen E, Heath PD, Holmes S, Holt K, Howden PJ, Hunt AR, Hunt SE, Hunter G, Isherwood J, James R, Johnson C, Johnson D, Joy A, Kay M, Kershaw JK, Kibukawa M, Kimberley AM, King A, Knights AJ, Lad H, Laird G, Lawlor S, Leongamornlert DA, Lloyd DM, Loveland J, Lovell J, Lush MJ, Lyne R, Martin S, Mashreghi-Mohammadi M, Matthews L, Matthews NS, McLaren S, Milne S, Mistry S, Moore MJ, Nickerson T, O'Dell CN, Oliver K, Palmeiri A, Palmer SA, Parker A, Patel D, Pearce AV, Peck AI, Pelan S, Phelps K, Phillimore BJ, Plumb R, Rajan J, Raymond C, Rouse G, Saenphimmachak C, Sehra HK, Sheridan E, Shownkeen R, Sims S, Skuce CD, Smith M, Steward C, Subramanian S, Sycamore N, Tracey A, Tromans A, Van Helmond Z, Wall M, Wallis JM, White S, Whitehead SL, Wilkinson JE, Willey DL, Williams H, Wilming L, Wray PW, Wu Z, Coulson A, Vaudin M, Sulston JE, Durbin R, Hubbard T, Wooster R, Dunham I, Carter NP, McVean G, Ross MT, Harrow J, Olson MV, Beck S, Rogers J, Bentley DR, Banerjee R, Bryant SP, Burford DC, Burrill WD, Clegg SM, Dhami P, Dovey O, Faulkner LM, Gribble SM, Langford CF, Pandian RD, Porter KM, Prigmore E (2006) The DNA sequence and biological annotation of human chromosome 1. *Nature* **441**: 315–321. doi:10.1038/nature04727.

Guyton JR, Klemp KF (1989) The lipid-rich core region of human atherosclerotic fibrous plaques. Prevalence of small lipid droplets and vesicles by electron microscopy. *Am J Pathol* **134**: 705–717.

Hassett C, Richter RJ, Humbert R, Chapline C, Crabb JW, Omiecinski CJ, Furlong CE (1991) Characterization of cDNA clones encoding rabbit and human serum paraoxonase: the mature protein retains its signal sequence. *Biochemistry* **30**: 10141–10149.

Herz J, Hamann U, Rogne S, Myklebost O, Gausepohl H, Stanley KK (1988) Surface location and high affinity for calcium of a 500-kd liver membrane protein closely related to the LDL-receptor suggest a physiological role as lipoprotein receptor. *EMBO J* **7**: 4119–4127.

Hiramatsu T, Sonoda H, Takanezawa Y, Morikawa R, Ishida M, Kasahara K, Sanai Y, Taguchi R, Aoki J, Arai H (2003) Biochemical and molecular characterization of two phosphatidic acid-selective phospholipase A1s, mPA-PLA1alpha and mPA-PLA1beta. *J Biol Chem* **278**: 49438–49447.

Hirata K, Dichek HL, Cioffi JA, Choi SY, Leeper NJ, Quintana L, Kronmal GS, Cooper AD, Quertermous T (1999) Cloning of a unique lipase from endothelial cells extends the lipase gene family. *J Biol Chem* **274**: 14170–14175.

Hjälm G, Murray E, Crumley G, Harazim W, Lundgren S, Onyango I, Ek B, Larsson M, Juhlin C, Hellman P, Davis H, Akerström G, Rask L, Morse B (1996) Cloning and sequencing of human gp330,

a $Ca^{2+}$-binding receptor with potential intracellular signaling properties. *Eur J Biochem* **239**: 132–137.
Hua X, Yokoyama C, Wu J, Briggs MR, Brown MS, Goldstein JL, Wang X (1993) SREBP-2, a second basic-helix-loop-helix-leucine zipper protein that stimulates transcription by binding to a sterol regulatory element. *Proc Natl Acad Sci USA* **90**: 11603–11607.
Ishii H, Kim DH, Fujita T, Endo Y, Saeki S, Yamamoto TT (1988) cDNA cloning of a new low-density lipoprotein receptor-related protein and mapping of its gene (LRP3) to chromosome bands 19q12-q13. 2. *Genomics* **51**: 132–135.
Ishii J, Adachi H, Aoki J, Koizumi H, Tomita S, Suzuki T, Tsujimoto M, Inoue K, Arai H (2002) SREC-II, a new member of the scavenger receptor type F family, trans-interacts with SREC-I through its extracellular domain. *J Biol Chem* **277**: 39696–39702.
Jacobs P, Cravador A, Loriau R, Brockly F, Colau B, Chuchana P, van Elsen A, Herzog A, Bollen A (1985) Molecular cloning, sequencing, and expression in Escherichia coli of human preprourokinase cDNA. *DNA* **4**: 139–146. doi:10.1016/0006-291X(89)91045-0.
Jenne DE, Tschopp J (1989) Molecular structure and functional characterization of a human complement cytolysis inhibitor found in blood and seminal plasma: identity to sulfated glycoprotein 2, a constituent of rat testis fluid. *Proc Natl Acad Sci USA* **86**: 7123–7127.
Kalchman MA, Graham RK, Xia G, Koide HB, Hodgson JG, Graham KC, Goldberg YP, Gietz RD, Pickart CM, Hayden MR (????) Huntingtin is ubiquitinated and interacts with a specific ubiquitin-conjugating enzyme. *J Biol Chem* **271**: 19385–19394.
Karathanasis SK, Yunis I, Zannis VI (1986) Structure, evolution, and tissue-specific synthesis of human apolipoprotein AIV. *Biochemistry* **25**: 3962–3970.
Karathanasis SK, Yunis I, Zannis VI (1986) Structure, evolution, and tissue-specific synthesis of human apolipoprotein AIV. *Biochemistry* **25**: 3962–3970.
Karathanasis SK, Yunis I, Zannis VI (1986) Structure, evolution, and tissue-specific synthesis of human apolipoprotein AIV. *Biochemistry* **25**: 3962–3970.
Kay LL, Ronan R, Schaefer EJ, Brewer HB, Jr (1982) Tangier disease: a structural defect in apolipoprotein A-I (apoA-I Tangier). *Proc Natl Acad Sci USA* **79**: 2485–2489.
Kim DH, Iijima H, Goto K, Sakai J, Ishii H, Kim HJ, Suzuki H, Kondo H, Saeki S, Yamamoto T (1996) Human apolipoprotein E receptor 2. A novel lipoprotein receptor of the low density lipoprotein receptor family predominantly expressed in brain. *J Biol Chem* **271**: 8373–8380.
Kluve-Beckerman B, Long GL, Benson MD (1986) DNA sequence evidence for polymorphic forms of human serum amyloid A (SAA). Biochem *Genet* **24**: 795–803.
Knott TJ, Priestley LM, Urdea M, Scott J (1984) Isolation and characterisation of a cDNA encoding the precursor for human apolipoprotein AII. *Biochem Biophys Res Commun* **120**: 734–740.
Knott TJ, Robertson ME, Priestley LM, Urdea M, Wallis S, Scott J (1984) Characterisation of mRNAs encoding the precursor for human apolipoprotein CI. *Nucleic Acids Res* **12**: 3909–3915.
Knott TJ, Wallis SC, Powell LM, Pease RJ, Lusis AJ, Blackhart B, McCarthy BJ, Mahley RW, Levy-Wilson B, Scott J (1986) Complete cDNA and derived protein sequence of human apolipoprotein B-100. *Nucleic Acids Res* **14**: 7501–7503.
Knowles TPJ, Vendruscolo M, Dobson Christopher MD (2014) The amyloid state and its association with protein misfolding diseases. *Nat Rev Mol Cell Biol* **15**: 384–396. doi:10.1038/nrm3810.
Koba S, Hirano T, Murayama S, Kotani T, Tsunoda F, Iso Y, Ban Y, Kondo T, Suzuki H, Katagiri T. (2003) Small dense LDL phenotype is associated with postprandial increases of large VLDL and remnant-like particles in patients with acute myocardial infarction. *Atherosclerosis* **170**: 131–40.
Kostner GM (1983) Apolipoproteins and lipoproteins of human plasma: significance in health and in disease. *Adv Lipid Res* **20**: 1–43.
Liu CX, Musco S, Lisitsina NM, Forgacs E, Minna JD, Lisitsyn NA (2000) LRP-DIT, a putative endocytic receptor gene, is frequently inactivated in non-small cell lung cancer cell lines. *Cancer Res* **60**: 1961–1967.
Magrane M. UniProt consortium (2011) UniProt Knowledgebase: a hub of integrated protein data Database bar009.
Mahley RW, Innerarity TL, Rall SC Jr, (1984) Weisgraber KH. Plasma lipoproteins: apolipoprotein structure and function. *J Lipid Res* **25**: 1277–1294.
Matsuguchi T, Okamura S, Aso T, Sata T, Niho Y (1989) Molecular cloning of the cDNA coding for proline-rich protein (PRP): identity of PRP as C4b-binding protein. *Biochem Biophys Res Commun* **165**: 138–144.
Matsumoto A, Naito M, Itakura H, Ikemoto S, Asaoka H, Hayakawa I, Kanamori H, Aburatani H, Takaku F, Suzuki H, et al (1990) Human macrophage scavenger receptors: primary structure, expression, and localization in atherosclerotic lesions. *Proc Natl Acad Sci USA* **87**: 9133–9137.
McLean J, Wion K, Drayna D, Fielding C, Lawn R (1986) Human lecithin-cholesterol acyltransferase gene: complete gene sequence and sites of expression. *Nucleic Acids Res* **14**: 9397–9406.
Minekura H, Fujino T, Kang MJ, Fujita T, Endo Y, Yamamoto TT (1997) Human acyl-coenzyme A synthetase 3 cDNA and localization of its gene (ACS3) to chromosome band 2q34-q35. *Genomics* **42**: 180–181.
Mörwald S, Yamazaki H, Bujo H, Kusunoki J, Kanaki T, Seimiya K, Morisaki N, Nimpf J, Schneider WJ, Saito Y (1997) A novel mosaic protein containing LDL receptor elements is highly conserved in humans and chickens. *Arterioscler Thromb Vasc Biol* **17**: 996–1002.
Morrisett JD, Jackson RL, Gotto AM Jr (1975) Lipoproteins: structure and function. *Annu Rev Biochem* **44**: 183–207.
Murdoch AD, Dodge GR, Cohen I, Tuan RS, Iozzo RV (1992) Primary structure of the human heparan sulfate proteoglycan from basement membrane (HSPG2/perlecan). A chimeric molecule with multiple domains homologous to the low density lipoprotein receptor, laminin, neural cell adhesion molecules, and epidermal growth factor. *J Biol Chem* **267**: 8544–8557.
Nakayama M, Nakajima D, Nagase T, Nomura N, Seki N, Ohara O (1998) Identification of high-molecular-weight proteins with multiple EGF-like motifs by motif-trap screening. *Genomics* **51**: 27–34.
Oelkers P, Behari A, Cromley D, Billheimer JT, Sturley SL (1998) Characterization of two human genes encoding acyl coenzyme A: cholesterol acyltransferase-related enzymes. *J Biol Chem* **273**: 26765–26771.
Oldfield CJ, Cheng Y, Cortese MS, Brown CJ, Uversky VN, Dunker AK (2005) Comparing and combining predictors of mostly disordered proteins. *Biochemistry* **44**: 1989–2000.
Olsson PA, Korhonen L, Mercer EA, Lindholm D (1999) MIR is a novel ERM-like protein that interacts with myosin regulatory light chain and inhibits neurite outgrowth. *J Biol Chem* **274**: 36288–36292.
Oquendo P, Hundt E, Lawler J, Seed B (1989) CD36 directly mediates cytoadherence of Plasmodium falciparum parasitized erythrocytes. *Cell* **58**: 95–101.
Ota T, Suzuki Y, Nishikawa T, Otsuki T, Sugiyama T, Irie R, Wakamatsu A, Hayashi K, Sato H, Nagai K, Kimura K, Makita H, Sekine M, Obayashi M, Nishi T, Shibahara T, Tanaka T, Ishii S, Yamamoto J, Saito K, Kawai Y, Isono Y, Nakamura Y, Nagahari K, Murakami K, Yasuda T, Iwayanagi T, Wagatsuma M, Shiratori A, Sudo H, Hosoiri T, Kaku Y, Kodaira H, Kondo H, Sugawara M, Takahashi M, Kanda K, Yokoi T, Furuya T, Kikkawa E, Omura Y, Abe K, Kamihara K, Katsuta N, Sato K, Tanikawa M, Yamazaki M, Ninomiya K, Ishibashi T, Yamashita H, Murakawa K, Fujimori K, Tanai H, Kimata M, Watanabe M, Hiraoka S, Chiba Y, Ishida S, Ono Y, Takiguchi S, Watanabe S, Yosida M, Hotuta T, Kusano J, Kanehori K, Takahashi-Fujii A, Hara H, Tanase TO, Nomura Y, Togiya S, Komai F, Hara R, Takeuchi K, Arita M, Imose N, Musashino K, Yuuki H, Oshima A, Sasaki N, Aotsuka S, Yoshikawa Y, Matsunawa H, Ichihara T, Shiohata N, Sano S, Moriya S, Momiyama H, Satoh N, Takami S, Terashima Y, Suzuki O, Nakagawa S, Senoh A, Mizoguchi H, Goto Y, Shimizu F, Wakebe H, Hishigaki H, Watanabe T, Sugiyama A, Takemoto M, Kawakami B, Yamazaki M, Watanabe K, Kumagai A, Itakura S, Fukuzumi Y, Fujimori Y, Komiyama M, Tashiro H, Tanigami A, Fujiwara T, Ono T, Yamada K, Fujii Y, Ozaki K, Hirao M, Ohmori Y, Kawabata A, Hikiji T, Kobatake N, Inagaki H, Ikema Y, Okamoto S, Okitani R, Kawakami T, Noguchi S, Itoh T, Shigeta K, Senba T, Matsumura K, Nakajima Y, Mizuno T, Morinaga M, Sasaki M, Togashi T, Oyama M, Hata H, Watanabe M, Komatsu T, Mizushima-Sugano J, Satoh T, Shirai Y, Takahashi Y, Nakagawa K, Okumura K, Nagase T, Nomura N, Kikuchi H, Masuho Y, Yamashita R, Nakai K, Yada T, Nakamura Y, Ohara O, Isogai T, Sugano S (2004) Complete sequencing and characterization of 21,243 full-length human cDNAs. *Nat Genet* **36**: 40–45.
Pannekoek H, Veerman H, Lambers H, Diergaarde P, Verweij CL, van Zonneveld AJ, van Mourik JA (1986) Endothelial plasminogen activator inhibitor (PAI): a new member of the Serpin gene family. *EMBO J* **5**: 2539–2544.
Pawlicki S, Le Béchec A, Delamarche C (2008) AMYPdb: a database dedicated to amyloid precursor proteins. *BMC Bioinformatics* **9**: 273. doi: 10.1186/1471-2105-9-273.
Pennica D, Holmes WE, Kohr WJ, Harkins RN, Vehar GA, Ward CA, Bennett WF, Yelverton E, Seeburg PH, Heyneker HL, Goeddel DV, Collen D (1983) Cloning and expression of human tissue-type plasminogen activator cDNA in *E. coli*. *Nature* **301**: 214–221.
Pepys MB (2006) Amyloidosis. *Annu Rev Med* **57**: 223–241.
Petersen CM, Nielsen MS, Nykjaer A, Jacobsen L, Tommerup N, Rasmussen HH, Roigaard H, Gliemann J, Madsen P, Moestrup SK (1997) Molecular identification of a novel candidate sorting receptor purified from human brain by receptor-associated protein affinity chromatography. *J Biol Chem* **272**: 3599–3605.
Polanco C, Buhse T, Samaniego JL, Castañón-González JA (2013) Detection of selective antibacterial peptides by the Polarity Profile method. *Acta Biochim Pol* **60**: 183–189.

Polanco C, Castañón-González JA, Samaniego JL (2014c) [Letter to the Editor] Arabi YM, Arifi AA, Balkhy HH, Najm H, Aldawood AS, Ghabashi A, Hawa H, Alothman A, Khaldi A, Raiy B (2014c) Clinical course and outcomes of critically Ill patients with middle east respiratory syndrome coronavirus infection. *Ann Intern Med* 2014 Jan 28. doi: 10.7326/M13–2486.

Polanco C, Samaniego JL (2009) Detection of selective cationic amphipatic antibacterial peptides by Hidden Markov models. *Acta Biochim Pol* **56**: 167–176.

Polanco C, Samaniego JL, Buhse T, Mosqueira FG, Negron-Mendoza A, Ramos-Bernal S, Castanon-Gonzalez JA (2012) Characterization of Selective Antibacterial Peptides by Polarity Index. *Int J Peptides* 58502. http://dx.doi.org/ 10.1155/2012/585027.

Polanco C, Samaniego JL, Castañón-González JA, Buhse T (2014a) Polar Profile of Antiviral Peptides from AVPpred Database. *Cell Biochem Biophys* **70**: 1469–1477. doi: 10.1007/s12013-014-0084-4.

Polanco C, Samaniego JL, Castañón-González JA, Buhse T, Sordo ML (2013a) Characterization of a possible uptake mechanism of selective antibacterial peptides. *Acta Biochim Pol* **60**: 629–633.

Polanco C, Samaniego-Mendoza JL, Buhse T, Castañón-González JA, Leopold-Sordo M (2014b) Polar Characterization of Antifungal Peptides from APD2 Database. *Cell Biochem Biophys* **70**: 1479–1488. doi: 10.1007/s12013-014-0085-3.

Polanco C, Castañón-González JA, Uversky VM (Letter to the Editor) Buhimschi IA, Nayeri UA, Zhao G, Shook LL, Pensalfini A, Funai EF, Bernstein IM, Glabe CG, Buhimschi CS (2014e) Protein misfolding, congophilia, oligomerization, and defective amyloid processing in preeclampsia. *Sci Transl Med* **6** (245): 245ra92. doi: 10.1126/scitranslmed. 3008808.

Polanco C, Samaniego-Mendoza JL, Castañón-González JA, Buhse T (Letter to the Editor) Howard SJ, Hopwood S, Davies SC (2014d) Antimicrobial Resistance: A Global Challenge. *Sci Transl Med* doi: 10.1126/scitranslmed. 3009315.

Primo-Parmo SL, Sorenson RC, Teiber J, La Du BN (1996) The human serum paraoxonase/arylesterase gene (PON1) is one member of a multigene family. *Genomics* **33**: 498–507.

Probst MR, Beer M, Beer D, Jenö P, Meyer UA, Gasser R (1994) Human liver arylacetamide deacetylase. Molecular cloning of a novel esterase involved in the metabolic activation of arylamine carcinogens with high sequence similarity to hormone-sensitive lipase. *J Biol Chem* **269**: 21650–21656.

Protter AA, Levy-Wilson B, Miller J, Bencen G, White T, Seilhamer JJ (1984) Isolation and sequence analysis of the human apolipoprotein CIII gene and the intergenic region between the apo AI and apo CIII genes. *DNA* **3**: 449–456.

Qing J, Wei D, Maher VM, McCormick JJ (1999) Cloning and characterization of a novel gene encoding a putative transmembrane protein with altered expression in some human transformed and tumor-derived cell lines. *Oncogene* **18**: 335–342.

Sawamura T, Kume N, Aoyama T, Moriwaki H, Hoshikawa H, Aiba Y, Tanaka T, Miwa S, Katsura Y, Kita T, Masaki T (1997) An endothelial receptor for oxidized low-density lipoprotein. *Nature* **386**: 73–77.

Scanu AM, Wisdom C (1975) Serum lipoproteins structure and function. *Annu Rev Biochem* **41**: 703–730

Shoulders CC, Brett DJ, Bayliss JD, Narcisi TM, Jarmuz A, Grantham TT, Leoni PR, Bhattacharya S, Pease RJ, Cullen PM, Levi S, Byfield PGH, Purskiss P, Scott J (1993) Abetalipoproteinemia is caused by defects of the gene encoding the 97 kDa subunit of a microsomal triglyceride transfer protein. *Hum Mol Genet* **2**: 2109–2116.

Shoulders CC, Kornblihtt AR, Munro BS, Baralle FE (1983) Gene structure of human apolipoprotein A1. *Nucleic Acids Res* **11**: 2827–2837.

Sipe JD, Colten HR, Goldberger G, Edge MD, Tack BF, Cohen AS, Whitehead AS (1985) Human serum amyloid A (SAA): biosynthesis and postsynthetic processing of preSAA and structural variants defined by complementary DNA. *Biochemistry* **24**: 2931–2936.

Stahnke G, Sprengel R, Augustin J, Will H (1987) Human hepatic triglyceride lipase: cDNA cloning, amino acid sequence and expression in a cultured cell line. *Differentiation* **35**: 45–52.

Stöhr H, Berger C, Fröhlich S, Weber BH (2002) A novel gene encoding a putative transmembrane protein with two extracellular CUB domains and a low-density lipoprotein class A module: isolation of alternatively spliced isoforms in retina and brain. *Gene* **286**: 223–231.

Strickland DK, Ashcom JD, Williams S, Battey F, Behre E, McTigue K, Battey JF, Argraves WS (1991) Primary structure of alpha 2-macroglobulin receptor-associated protein. Human homologue of a *Heymann nephritis* antigen. *J Biol Chem* **266**: 13364–13369.

Thom R (1952) Espaces fibrés en sphères et carrés de Steenrod. Annales Scientifiques de l'École Normale Supérieure **69**: 109–182.

Timberlake, KC, Chemistry – 5th edn, Haper-Collins Publishers Inc, NY, 1992, accessed May 16, 2014 http://www.ann.com.au/MedSci/amino.htm.

Tjoelker LW, Wilder C, Eberhardt C, Stafforini DM, Dietsch G, Schimpf B, Hooper S, Le Trong H, Cousens LS, Zimmerman GA, Yamada Y, McIntyre TM, Prescott SM, Gray PW (1995) Anti-inflammatory properties of a platelet-activating factor acetylhydrolase. *Nature* **374**: 549–553.

Uversky VN (2002) Natively unfolded proteins: a point where biology waits for physics. *Protein Sci* **11**: 739–756.

Uversky VN (2009) Intrinsic disorder in proteins associated with neurodegenerative diseases. *Frontiers in Bioscience* **14**: 5188–5238;

Uversky VN (2010) Targeting intrinsically disordered proteins in neurodegenerative and protein dysfunction diseases: Another illustration of the D2 concept. *Expert Review of Proteomics* **7**: 543–564.

Uversky VN (2014) The triple power of D3: Protein intrinsic disorder in degenerative diseases. *Frontiers in Bioscience* **19**: 181–258.

Uversky VN, Fink AL (2004) Conformational constraints for the amyloid fibrillation: The importance of being unfolded. *Biochim Biophys Acta* **1698**: 131–153.

van der Vliet HN, Sammels MG, Leegwater AC, Levels JH, Reitsma PH, Boers W, Chamuleau RA (2001) Apolipoprotein A-V: a novel apolipoprotein associated with an early phase of liver regeneration. *J Biol Chem* **276**: 44512–44520.

Whitehead AS, de Beer MC, Steel DM, Rits M, Lelias JM, Lane WS, de Beer FC (1992) Identification of novel members of the serum amyloid A protein superfamily as constitutive apolipoproteins of high density lipoprotein. *J Biol Chem* **267**: 3862–3867.

Whitney GS, Chan PY, Blake J, Cosand WL, Neubauer MG, Aruffo A, Kanner SB (1993) Human T and B lymphocytes express a structurally conserved focal adhesion kinase, pp125FAK. *DNA Cell Biol* **12**: 823–830.

Wion KL, Kirchgessner TG, Lusis AJ, Schotz MC, Lawn RM (1987) Human lipoprotein lipase complementary DNA sequence. *Science* **235**: 1638–1641.

Xu N, Dahlbäck B (1999) A novel human apolipoprotein (apoM). *J Biol Chem* **274**: 31286–31290.

Yamamoto T, Davis CG, Brown MS, Schneider WJ, Casey ML, Goldstein JL, Russell DW (1984) The human LDL receptor: a cysteine-rich protein with multiple Alu sequences in its mRNA. *Cell* **39**: 27–38.

Yokoyama C, Wang X, Briggs MR, Admon A, Wu J, Hua X, Goldstein JL, Brown MS (1993) SREBP-1, a basic-helix-loop-helix-leucine zipper protein that controls transcription of the low density lipoprotein receptor gene. *Cell* **75**: 187–197.

Yoshikawa T, Sanders AR, Esterling LE, Detera-Wadleigh SD (1998) Multiple transcriptional variants and RNA editing in C18orf1, a novel gene with LDLRA and transmembrane domains on 18p11.2. *Genomics* **47**: 246–257.

Zannis VI, McPherson J, Goldberger G, Karathanasis SK, Breslow JL. (1984) Synthesis, intracellular processing, and signal peptide of human apolipoprotein E. *J Biol Chem* **259**: 5495–5499.