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Proteomics and the Eye

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In the post-genomic era, recent advances in protein chemistry, mass spectrometry, and bioinformatics are bringing a rapid and fundamental transformation to biological and medical research. In humans, ~20,000 protein-coding genes give rise to ~100,000 proteins and an estimated 1 million different protein modified forms [1]. The proteome, which consists of all proteins expressed in a cell, tissue, or organism, is the basic link between the genome and phenotypes of health and disease. Proteins function as enzymes, hormones, receptors, immune mediators, structure, transporters, and modulators of cell communication and signaling. The many forms of proteins arise from mutations, RNA editing, RNA splicing, and post-translational modification – the proteome has much greater complexity than the genome. A major goal of proteomics is to detect and measure the diversity of proteins, their isoforms, and the localization and interactions of proteins in order to discover biological mechanisms, biomarkers, drug targets, and pathways of disease. Proteomics is a vital step in the progress of science from genetics to proteomics and subsequently to translational research and clinical trials.

Proteomics has come relatively late to the field of ophthalmology and vision science compared with areas such as cancer, cardiovascular, and neurology research. The eye is an emerging proteome that offers many new opportunities for discovery [2]. In this Focus issue, several groups of investigators present research and perspectives on proteomics and its applications to the understanding of eye disease. Primary open angle glaucoma is a leading cause of blindness and the subject of three papers in this issue. Sienkiewicz and colleagues used isobaric tags for relative and absolute quantitation (iTRAQ) to compare the proteome of the trabecular meshwork in eyes with and without glaucoma. Glycosylation, an important post-translational modification (PTM), was altered in the trabecular meshwork of subjects with glaucoma [3]. Bouhenni and Edward provide a useful overview of proteins found in anterior segment tissues that have been associated with different types of glaucoma [4]. For over a decade, Tezel has conducted proteomic investigations of glaucoma, with a focus on the posterior segment of the eye and glaucomatous neurodegeneration. She draws from her experiences to show the different approaches her group has taken to identify altered protein expression, PTMs, and protein interactions in experimental glaucoma [5].

Corneal dystrophies, which can lead to visual disability and blindness, must often be treated by penetrating keratoplasty. The corneal dystrophies that are associated with variants of

transforming growth factor beta induced protein (TGFBIp) are not well understood. Poulsen and colleagues investigated differences in lattice corneal dystrophy type 1 caused by A546D substitution versus A546D/P551Q double substitution. The P551Q mutation had altered thermodynamic stability that accounted for the structural changes in TGFBIp [6]. Limbal stem cells are essential for regeneration of the cornea epithelium. Honoré and Vorum review the limited work to date on stem cell markers and emphasize the need for proteomic approaches to understand limbal stem cell biology [7]. The tear film is a readily accessible fluid for biomarker analysis. Salvisberg and colleagues found a consistent association between elevated alpha-1 antichymotrypsin in tears and multiple sclerosis [8].

The human lens contains proteins that do not turn over during the lifespan. Truscott and Friedrich review the accumulation of PTMs and degradation of lens proteins with aging [9]. It is interesting to note that age-related changes in lens crystallins begin as early as the second decade of life. The vitreous may provide valuable clues to the pathogenesis of retinal diseases. In their Viewpoint, Mahajan and Skeie emphasize the potential that the vitreous proteome may have in the future for personalized therapeutics [10]. The systematic collection of eye tissues is fundamental for high quality scientific investigation. Skeie and associates describe a platform for the collection and storage of biological samples for proteomic studies [11].

O-GlcNAcylation, the addition of a single *O*-GlcNAc moiety to the hydroxyl and serine residues of proteins, was discovered in 1984 by Torres and Hart [12]. This basic and dynamic PTM is implicated in diabetic retinopathy. Hyperglycemia increases flux through the hexosamine biosynthetic pathway, which, in turn, upregulates *O*-GlcNAcylation. The number of tools to study *O*-GlyNAcylation is increasing and should facilitate our understanding of diabetic retinopathy [13].

Proteomic investigations of the eye show the great potential of proteomics in providing novel insights into the pathogenesis of specific eye diseases. In the recent literature, Feener and associates showed that the kallikrein kinin system plays a role in the increased vascular permeability that occurs in diabetic retinal edema [14]. Chaekady and colleagues used iTRAQ and LC-MS/MS to identify proteins that were increased and decreased in the corneal stroma in keratoconus [15]. Descriptive studies of the cornea [16], tear film [17], and ciliary body [18] have greatly increased the known proteome of the human eye.

In order to facilitate further work on the proteome of the human eye, the Human Eye Proteome Project (HEPP) was founded in September 2012 as a component of the Biology/Disease-driven Human Proteome Project of the Human Proteome Organization [2]. The audacious goal of the HEPP is “to characterize the proteome of the human eye in health and disease in order to gain insight into the pathophysiology of eye diseases and to contribute to new preventive and therapeutic modalities for the prevention of visual disability and blindness” [2]. We hope that this collection of papers “Focus on Proteomics and the Eye” will help stimulate further exciting work in this rapidly expanding area of investigation.

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References

1. Hood LE, Omenn GS, Moritz RL, Aebersold R, Yamamoto KR, Amos M, Hunter-Cevera J, Locascio L. New and improved proteomics technologies for understanding complex biological systems: addressing a grand challenge in the life sciences. *Proteomics*. 2012; 12:2273–2783.
2. Semba RD, Enghild JJ, Venkatraman V, Dyrland TF, Van Eyk JE. The Human Eye Proteome Project: perspectives on an emerging proteome. *Proteomics*. 2013; 13:2500–2511. [PubMed: 23749747]
3. Sienkiewicz AE, Rosenberg BN, Edwards G, Carreon TA, Bhattacharya SK. Aberrant glycosylation in the human trabecular meshwork. *Proteomics Clin. Appl.* 2014 [In this issue].
4. Bouhenni RA, Edward DP. Proteome of the anterior segment structure in relation to glaucoma. *Proteomics Clin. Appl.* 2014 [In this issue].
5. Tezel G. A decade of proteomics studies of glaucomatous neurodegeneration. *Proteomics Clin. Appl.* 2014 [In this issue].
6. Poulsen ET, Runager K, Risør MW, Dyrland TF, Scavenius C, Karring H, Praetorius J, Vorum H, Otzen DE, Klintworth GK, Enghild JJ. Comparison of two phenotypically distinct lattice corneal dystrophies caused by mutations in the transforming growth factor beta induced (TGFB1) gene. *Proteomics Clin. Appl.* 2014 [In this issue].
7. Honoré B, Vorum H. Proteomic analysis as a means to approach limbal stem cell biology in a search for stem cell markers. *Proteomics Clin. Appl.* 2014 [In this issue].
8. Salvisberg C, Tajouri N, Hainard A, Burkhard PR, Lalive PH, Turck N. Exploring the human tear fluid: discovery of new biomarkers in multiple sclerosis. *Proteomics Clin. Appl.* 2014 [In this issue].
9. Truscott RJ, Friedrich MG. Old proteins and the Achilles heel of mass spectrometry. The role of proteomics in the etiology of human cataract. *Proteomics Clin. Appl.* 2014 [In this issue].
10. Mahajan VB, Skeie JM. Translational vitreous proteomics. *Proteomics Clin. Appl.* 2014 [In this issue].
11. Skeie JM, Tsang SH, Zande RV, Fickbohm MM, Shah SS, Vallone JG, Mahajan VB. A biorepository for ophthalmic surgical specimens. *Proteomics Clin. Appl.* 2014 [In this issue].
12. Torres CR, Hart GW. Topography and polypeptide distribution of terminal *N*-acetylglucosamine residues on the surfaces of intact lymphocytes. Evidence for *O*-linked Glc-NAc. *J. Biol. Chem.* 1984; 259:3308–3317. [PubMed: 6421821]
13. Semba RD, Huang H, Luttly GA, Van Eyk JE, Hart GW. The role of *O*-GlcNAc signaling in the pathogenesis of diabetic retinopathy. *Proteomics Clin. Appl.* 2014 [In this issue].
14. Gao BB, Clermont A, Rook S, Fonda SJ, Srinivasan VJ, Wojtkowski M, Fujimoto JG, Avery RL, Arrigg PG, Bursell SE, Aiello LP, Feener EP. Extracellular carbonic anhydrase mediates hemorrhagic retinal and cerebral vascular permeability through prekallikrein activation. *Nat. Med.* 2007; 13:181–188. [PubMed: 17259996]
15. Chaerkady R, Shao H, Scott SG, Pandey A, Jun AS, Chakravarti S. The keratoconus corneal proteome: loss of epithelial integrity and stromal degeneration. *J. Proteomics*. 2013; 87:122–131. [PubMed: 23727491]
16. Dyrland TF, Poulsen ET, Scavenius C, Nikolajsen CL, Thøgersen IB, Vorum H, Enghild JJ. Human cornea proteome: identification and quantification of the proteins of the three main layers including epithelium, stroma, and endothelium. *J. Proteome Res.* 2012; 11:4231–4239. [PubMed: 22698189]
17. Zhou L, Zhao SZ, Koh SW, Chen L, Vaz C, Tanavde V, Li XR, Beuerman RW. In-depth analysis of the human tear proteome. *J. Proteomics*. 2012; 75:3877–3885. [PubMed: 22634083]

18. Goel R, Murthy KR, Srikanth SM, Pinto SM, Bhattacharjee M, Kelkar DS, Madugundu AK, Dey G, Mohan SS, Krishna V, Prasad TSK, Charavarti S, Harsha HC, Pandey A. Characterizing the normal proteome of human ciliary body. *Clin. Proteomics*. 2013; 10:9. [PubMed: 23914977]

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