Peeking into the molecular trove of discarded surgical specimens

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When you next sit down and hear the gentle whir of phacoemulsification or discard tissue following extraocular muscle resection, ask yourself “what insights into this patient’s pathological process have now been lost forever?” The difficulty in obtaining ocular tissue from living people represents a significant barrier to studying both common and rare ophthalmic diseases. However, with adequate access to well-characterised ocular specimens, the ever sharper tools for biological discovery can be aptly applied to dissect disease pathogenesis.

Cell or tissue specific perturbations at the genomic (*i.e.* DNA), epigenetic, transcriptomic (*i.e.* RNA), or even proteomic level can lead to disease, and given that these disease-specific variations can manifest or arise solely in affected ocular cells, the direct profiling of ocular specimens is paramount to an improved understanding of pathogenesis. Retinoblastoma is the archetypal ophthalmic disease which manifests, either solely or in part, due to somatic mutations.¹ Consequently, DNA sequencing of retinoblastoma tumour specimens can have important ramifications for ongoing screening of the individual patient and their family members.

Khong *et al.* have recently investigated the gene expression profile of orbital adipose tissue in patients with active, inactive or no thyroid orbitopathy.² They found that active thyroid orbitopathy is characterized by upregulation of genes involved in cell-mediated immune, innate immune, and inflammatory response.² The top differentially expressed genes implicated through this work could have only been identified through the direct study of surgical specimens.

Direct mass spectrometry of pseudoexfoliation material collected during phacoemulsification surgery identified a predominance of LOXL1 protein.³ Intriguingly, this would have been a novel discovery had these surgical specimens been interrogated before any blood-based genetic research had been undertaken into this disease.⁴ Even undiluted

vitreous samples collected from patients at the time of pars plana vitrectomy have been used to identify proteomic signatures of proliferative diabetic retinopathy.⁵

In this issue, Seet and colleagues report iris gene expression profiles in specimens obtained from patients undergoing trabeculectomy for treatment of either primary angle closure glaucoma (PACG) or primary open angle glaucoma (POAG).⁶ They identified an expression profile in POAG and PACG irises which not only distinguished the two subtypes, but also improved the accuracy of their description when combined with known biometric characteristics. Although there are important limitations of this work, such as the fact that only a small number of candidate gene transcripts were interrogated and the inability to attribute cause or effect, this study does highlight the potential utility of surgical specimens, which are typically discarded, and presents a call-to-arms for enrolling a larger number of subjects for simultaneous tissue and biometric analyses.

Understanding the precise molecular mechanisms leading to blinding disease will, in time enable improved screening programmes and the development of novel therapies.⁷ Although much insight into the molecular mechanisms of many ophthalmic diseases has been achieved, further work is required and one of the richest troves for ongoing research will continue to come from discarded surgical specimens.

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