001. Barry Firkin Oration: Well within 6 degrees of separation: From ristocetin to collagen binding and beyond.

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Barry Firkin was an esteemed and respected scientist in the field of haematology with a broad clinical and academic interest. One of his most marked achievements, however, was the discovery that ristocetin promoted platelet aggregation in a von Willebrand factor (VWF) dependent manner, paving the way for the development of several diagnostic assays based on this finding. Undeniably, the ristocetin induced platelet aggregation (RIPA) and VWF ristocetin cofactor (VWF:RCo) assays are now part of the standard repertoire of laboratory tests for identification or exclusion of von Willebrand disease (VWD), in turn the most common bleeding disorder (arising from defects or deficiency of VWF). Indeed, VWF:RCo is still today considered the surrogate gold standard 'functional' or VWF 'activity' assay in VWD diagnostics. This presentation will explore VWD diagnostics, in part as a historical journey, and reflect on the many milestones and changes over recent decades. One milestone along this journey, for example, was the development of the VWF collagen binding (VWF:CB) assay as a second 'functional' or VWF activity assay in VWD diagnostics. Rather than being a replacement for VWF:RCo, the VWF:CB is seen as a supplementary assay that reflects a surrogate of one function of VWF, namely subendothelial matrix adhesion, as part of the process of attaching platelets to damaged tissue, and subsequent thrombus formation. The VWF:RCo, in turn, reflecting a surrogate of a complementary function of VWF, being platelet adhesion, as part of the process of facilitating platelets to attach to each other and to damaged tissue, and thus also aiding subsequent thrombus formation. More recently, this functional surrogate of VWF binding to platelets, aka the classical VWF:RCo assay, has been morphed into a variety of 'glycoprotein Ib (GPIb) – binding assays', and has even spawned a new ISTH SSC recommended nomenclature, including terms such as VWF:GPIbR and VWF:GPIbM. These are assays that may or may not use ristocetin, and generally do not even use platelets.