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this paper describes the development of an immunohistochemical assay, using the amino-terminal peptide of poly(a) polymerase (pap) as a specific marker for pap, as well as a quantitative reverse transcription-polymerase chain reaction (rt-pcr) method to measure the expression of pap and other rna polymerases. the findings are discussed in the wider context of biophysical calculations applied to the family of epo orthologues, yielding a diverse range of calculated values. it is suggested that combining such calculations with naturally-occurring sequence variation, and 3d model generation, could lead to a valuable tool for protein solubility design. to define the molecular components responsible for the close contact of pcs and ecs, we analyzed the expression of several molecules in murine tissues by immunohistochemistry. initially, we examined the expression of platelet-derived growth factor receptor-β (pdgfrβ) in vessels with pcs. pdgfrβ is a cell surface protein that is expressed by pcs in mature vessels [5]. we found pdgfrβ localized at the cellular junctions between pcs and ecs in mouse retina, and pdgfrβ-positive pcs were also identified in the cerebral cortex, but not in cerebellum and spinal cord (figure 1 b c). to further characterize the expression of pdgfrβ, we examined the expression of pdgfrβ in vivo by using embryonic stem cells (escs) that differentiated into ecs, pcs, or both. e14.5 escs differentiated into ecs and pcs in vitro, and we cultured these cells with each other in vitro to assess the molecular interactions between pcs and ecs. we confirmed the expression of pdgfrβ in pcs and ecs by immunohistochemistry and western blotting (figure 1 d a). figure 1. in situ expression of pdgfr in pcs, ecs and vascular cells. (a) e14.5 escs were cultured under differentiation conditions as described in the text. differentiated cells were fixed and immunolabeled against pdgfr (magenta) and laminin (green), a basement membrane marker. (b) e14.5 escs differentiated into ecs and pcs in vitro.5 escs were cultured as described in the text and fixed and immunolabeled against pdgfr and laminin. ecs, which were identified by laminin (green) and cd31 (magenta), expressed pdgfr in both whole mounts and cultured cells. (c) pdgfr-positive pcs were identified by their morphology in whole mounts and cultured cells. (d) pdgfr-positive pcs were identified by their morphology in whole mounts and cultured cells. (online version in colour.)

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resultswork by us and others demonstrates that biomaterials are key to the treatment of various diseases such as cancer, heart disease, alzheimer's, parkinson's disease, arthritis, muscular dystrophy, and eye disease. biomaterials are defined as "natural or man-made solid, semisolid or liquid biocompatible materials designed to interact with biological systems." these novel biomaterials are being used to design and develop new medical devices that restore and maintain the functions of human tissues. these advances are being made in the areas of catheters, stents, pacemakers, contact lenses, and sensors. it is difficult to predict which biomaterial design will prove to be most successful and thus our future success relies on our ability to precisely measure the mechanical properties of the materials at both the nanoscale and microscale level. for example, prior to implantation of a medical device, it is necessary to know the dynamic behavior of the device when exposed to the specific tissue environment. for example, implantation of a stent into a coronary artery requires that the stent can withstand the mechanical stresses of pulsatile blood flow within the artery without causing excessive damage to the wall or causing an acute thrombosis at the site of stent implantation. we have used atomic force microscopy (afm) to investigate the dynamic behavior of medical devices during nano- to microscale mechanical testing of small amounts of material, usually less than 1 mg. methods such as afm are suitable for characterizing the dynamic behavior of a material over a wide range of spatial scales. this has become a new way to characterize the mechanical properties of materials at both the nanoscale and the microscale level. we will highlight several of our recent results with a special emphasis on the various afm methods that we have used to characterize our biomaterials. we will also illustrate the potential of afm in the future for the development of nanoscale pharmaceuticals, biomaterials, and other materials. 5ec8ef588b

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