ABSTRACT: Interactions at the implant-tissue interface are driven by the topography and chemistry of the surface. The diversity of surface treatments available on commercial implants indicates that an optimum surface has not yet been identified. Because implants chemistry has been more or less limited to Ti and its alloys, altering the topography of the surface is perhaps the most effective means of optimizing the tissue-implant interface so that cell responses can be directed along desired pathways. We have studied the effects of topography on cell behaviour using microfabricated surfaces produced by techniques used in the microelectronics industry as well as surfaces produced by industrial processes such as grit blasting or acid etching. Both types of surface can be replicated in epoxy, coated with Ti and used as substrata for cell culture or implanted in vivo. Rough surfaces affect macrophage signaling pathways that are known to control cytokine release and thus allow a way to modulate wound healing around the implant. In a rat model immunohistochemical studies demonstrated that rough surfaces attract recruited (i.e. ED-1 positive) macrophages and detailed Transmission Electron Microscopic observations suggest that the mineralization adjacent to implant surfaces resembles in some aspects other ectopic mineralization processes such as atherosclerosis. Osteoblast response to specific topographical features in vitro requires FAK-Src complexes for activation whereas on smooth surfaces FAK-Src independent pathways for ERK 1/2 activation are present. That specific cell signaling pathways can be activated by specific topographies suggests that detailed studies are required that link the size, shape and spacing of topographical features to diverse cell signaling cascades.