Electronic Supplementary Material (ESI) for Biomaterials Science.
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Supplementary Table 1. Summary of the *in vitro* studies included in the systematic review

TESTED MATERIALS	CELL TYPE	PERFORMED TESTS and EXPERIMENTAL TIMES	MAIN OUTCOME	MAIN CONCLUSION	REF
			CELLs FROM SKIN ORIGIN		
Medical grade poly (ε-caprolactone) scaffold realized with melt electrowriting (MEW) technique in comparison with: - un-seeded tubular scaffolds - solid PCL tubes	Human dermal fibroblasts (HDF)	Confocal laser scanning microscope and SEM at 4 days; Cell viability at 4 days; Cell proliferation at 4 and 7 days. Histological evaluation after insertion in reconstructed Human Skin Equivalent models at 3, 7 and 12 days Pullout testing 12 days after HSE insertion	Cells elongation and sheet formation after 4 days 90% of cells viability and increasing proliferation values from 4 to 7 days. Different epidermal growth patterns around the PCL samples: At day 3, 2 solid PCL out of 4 samples exhibited epidermal downgrowth. At day 7, 3 out of 4 samples exhibited epidermal downgrowth and at day 12, 4 out of 6 samples exhibited epidermal downgrowth. All un-seeded samples exhibited epithelial downgrowth at all-time points; The majority of the pre-seeded samples exhibited epithelial up-growth: at day 3, 3 out of 5 samples exhibited signs of epidermal up-growth, 6 out of 6 at day 7 and 3 out of 5 at Day 12. Pre-seeded and un-seeded implants exhibited similar mean maximum pullout forces of 0.498 N ± 0.067 N and 0.538 N ± 0.055 N, respectively	MEW technique is useful to modified surface encouraging skin integration	Bolle, 2020

			Solid PCL exhibit a ↓ maximum pullout force of 0.076 N ± 0.032 N.		
Silicon surface coated with Ti nanocoating further immersed in a polydopamine coating. Four study group: - milli-Q water storing (PDA); - protein A incubation prior to the functionalization with the extracellular domain of human E-cadherin fused with the Fc domain of human IgG producing an alignment orientation (ProtA-EcadFc); - direct incubation with EcadFc in a random orientation; - incubation with fibronectin (PDA-FN).	HaCaT cells (keratinocytes) and primary dermal fibroblast	Adhesion and Proliferation at 4, 24 and 48 hrs Migration test for 24 hrs	HaCaTs adhesion and spreading on all surfaces with no differences in cell numbers at 4 hrs. ↑ HaCaT on PDA-FN *vs* PDA. at 24 hrs ↑ HaCaT on PDA-FN *vs* protA-EcadFc at 48 hrs No proliferation at 48 hrs on PDA and PDA-protA-EcadFc. ↓ cell area for PDA-protA-EcadFc vs other coatings at 4 hrs ↑ cell area for PDA-protA-EcadFc, at 24- and 48 hrs vs PDA-FN at 48 hrs. ↑ migration rate for PDA-FN substrates and ↓ for PDA-protA-EcadFc at 24 hrs. ↓ adhesion of fibroblast on PDA-protA-EcadFc substrate, while ↑ adhesion for PDA and PDA-FN at 4 hrs.	HaCaTs attached to the surfaces even if a decrease in cells proliferation and increase in cell size was present on aligned surfaces (ProtA-EcadFC). The aligned E-cadherin surface was non-adhesive for primary human dermal fibroblasts. E-cadherin functionalization could be useful in percutaneous implants to ensure epidermal attachment, limit epidermal downgrowth and prevent fibroblast adhesion	Dehli, 2019
Ti discs (grade 2) and grade 1 Ti film as control material *vs* materials submitted to two different alkali-heat (AH) treatments (5 or 10 M AH treatment) in order to realized nano-topographic (nano-spike and nano-pores) surfaces	HDF	Cellular morphology and adhesion at 1 day Cells viability at 1 and 7 days Gene expression at 14 days	Fibroblasts onto machined surface were spindle shapes with well-developed and unidirectional actin formation and lamellipodia; Fibroblast on 5M AH- were small but with spotty/circular actin accumulation inside and	The nano-topographies of the AH-treated surfaces were able to stimulate fibroblast adhesion, proliferation and ECM production.	Yamada, 2016

		Collagen production at 28 days Inflammatory cytokines detection at 3 days SEM at 28 days	at the edge of the cells. On 10 M AH, cells were rectangular, spindle, or oval shapes with a cytoskeletal network with multiple orientations, and actin accumulation. ↓ Cell viability on treated surfaces *vs* the machined ones at day 1, non-differences at day 4. ↑ collagen deposition on treated surfaces (fold 1.2 for 5 M and 1.7 for 10 M) vs machined surfaces ↑ up-regulation of COL1 and 3, FBN and ELN on treated surfaces vs machined no differences among surfaces for cytokines levels (GM- CSF, IFN-γ, IL-1β, -6 and -8, MCP-1 and -3, M-CSF)		
Ti Nano-tubed (TNT) obtained with anodization vs polished Titanium (pTi)	Human epidermal keratinocytes (HaCat) and human dermal fibroblasts (HDF) used in 5 experimental groups: 1) HaCat (K) cells seeded on TNT or pTi surfaces. 2) F: HDF (F)	Cells proliferation and morphology at 1, 3 and 7 day Gene expression at 4, 24 and 72 hrs Immunofluorescence assay at 7 days	↑ viability of HaCat cells at 3 and 7 days in single culture on pTi *vs* HaCat cells cultured on TNT. ↓ proliferative activity in group 3 especially onto pTi at 7 days *vs* single cultures. HaCat appeared cuboidal, non-elongated and aggregated on the surfaces. ↑ HaCat adhesion on pTi surface than TNT at 7 days	Better orientation of HSF cells on the TNT and decreased adhesion and proliferation of HaCat. The TNT surface was beneficial to the fibroblasts, but unsatisfactory for keratinocytes in both single culture and non-contact co-culture.	Tan, 2017

	cells seeded on TNT or pTi surfaces. 3) K/F: HaCat cells on material surfaces non-contact co-cultured with HDF cells. 4) F/K: HDF cells on material surface were non-contact co-cultured with HaCat cells. HDF cells were seeded on TNT or pTi surface, and then HaCat cells were seeded on the transwell. 5) Co: The two types of cells were contact co-cultured on material surfaces (contact cultures).		and ↓ in group 3 onto both pTi and TNT ↑ expression level of laminin-β3 by HaCat cells and Collagen IVα-1 for both cell type in single culture on the pTi surface *vs* TNT; ↓ laminin- β3 on TNT and pTi surfaces in group 4 and ↓ level of collagen IVα-1 in HaCat cells on TNT in group 3 *vs* single culture. ↑ HDF cell density in single culture on TNT surface *vs* pTi at 3 and 7 days and also in group 4. ↑ proliferative activity of HSF cells in group 4 *vs* single cultures. HDF morphology was elongated and spindle-like shape at 7 d. ↑ HDF adhesion on TNT surface and better orientation in group 4 ↑ TGF-β1 and Collagen IVα-1 expression by HDF cells in single cultures and in group 3 on TNT surface *vs* pTi. ↑ collagen I and collagen IV expression by HDF in group 4.		
Titanium alloy (Ti–6Al–4V) polished disks evaluated in	Human fibroblasts	Cells Morphology at 24 hrs	Larger, flatter and more spread out cells on surfaces coated	Fn coatings exert a positive effect on	Chimutengwende-Gordon, 2011*

10 conditions: - polished (Pol); - silanized alone (Si); - passivated for the 2 h period (120 Pass); - passivated for a reduced time period of 5 min (5 Pass); - silanized following passivation for 2 h (120 PassSi); - silanized following passivation for 5 min (5 PassSi); - adsorbed fibronectin (AdFn); - SiFn following 2 h passivation (120 PassSiFn); - SiFn following 5 min passivation (5 PassSiFn) and - SiFn without passivation	(1BR3G)	Adhesion and area quantification by Immunohistochemistry (anti-vinculin) at 24 hrs Cells Metabolism at 24 hrs	with Fn. Cells on Si ↑spread out *vs* Pol discs. ↑ filopodia on AdFn, SiFn and 5 PassSiFn and cell–cell interactions *vs* 120 PassSiFn and control discs. ↓ fewer, smaller and low adhesion on passivated surfaces for 24 hrs. ↓ adhesion plaques for cells on passivated and silanized surfaces *vs* SiFn. ↑ vinculin markers for SiFn *vs* 5 PassSiFn and 120 PassSiFn and polished disks. ↑ adhesion when Fn is present, irrespective of the silanized, adsorbed or passivated surfaces. ↑ cells size and vinculin markers on the Fn-coated substrates irrespective of coating regime.	fibroblast adhesion. Passivation is detrimental to fibroblast adhesion even for short periods of time Fn coating overcome the negative effect of passivation and or silanization on wettability	
Ti coated glass silanized with different agents with nano-keratin coatings extracted from human hair fibers: - keratose (KOS) - Kerateine (KTN) Or with - Fibronectin (FN)	Human neonatal primary dermal fibroblast (PCS-201-010) and human keratinocytes HaCaT cells	Focal adhesion immunocytochemistry at 30 min, 1 and 3 hrs Detection of smooth muscle actin (SMA) in fibroblast at 3 hrs Detection of involucrin in	Rounded shape on all substrates at 30 min for fibroblast Flattened morphology and enlargement at 1 hr for FN, and spreading and filopodia for KTN substrate.	Keratin seem to represent an attractive biomimetic coating (simulating human fingernail) for the percutaneous component	Trent, 2019

- Collagen type I - Plain titanium (pTi)		HaCaTs at 3 hrs, 1 and 7 days	Branched morphology on KOS and KTN substrates *vs* polygonal shape on pTi, and aFN Good adhesion for HaCaT cells to all substrates with branched filopodia on the keratin substrates. Slight staining for SMA in fibroblasts on all substrates at all times points. ↑ positive staining for involucrin in HaCaT cells on KTN and KOS.		
Polished surgical grade Ti alloy (Ti-6Al-4V) used as controls (Pol) in comparison with non-Fn-functionalized sintered HA discs (HA) and HA-Fn functionalization (HAFn)	Human dermal fibroblasts (1BR3G)	Focal adhesion at 1, 4 and 24 hrs Cell area quantification at 1 4 and 24 hrs	↑ Focal adhesion on HAFn *vs* HA and Pol controls at all time-points. ↑ Cell area at 1 and 4 hrs on HA < Pol < HAFn, at 24 hrs the cell areas on HAFn and Pol were significantly greater than on HA. ↑ Attachment on HAFn than on HA at four and 24 hrs	Fn-coated HA implants may improve dermal tissue adhesion in osteointegrated implant	Pendegrass, 2012a
Ground and polished Ti alloy with a surface roughness of about 0.03 Ra, with different surface configurations: - polished discs (Pol), - polished discs with absorbed fibronectin (AdFn), - polished disc which were silanized (Si) and - polished discs that were	Immortalized Human dermal fibroblasts (1BR3G)	Focal adhesion (FA) immunolocalization at 1, 4, 24, and 96 hrs. Cell areas, vinculin counts at 1,4, 24 and 96 hrs Shear stress for 24 hrs	↑ Shear stress and FA density between 1 and 24 hrs for Pol ↓ Shear stress between time points but no significant differences in FA density for AdFN and SiFn. ↑ cell area between time points for AdFN and SiFn.	Dermal fibroblast attachment strength is significantly improved by fibronectin coating in comparison with uncoated Titanium	Pendegrass, 2010

silanized and treated with fibronectin (SiFn).			↑ Shear stress and FA density significantly increased between 1 and 24 hrs for Si At 1 hour: ↑shear stress and FA density for adsorbed Fn substrates *vs* uncoated control (Pol *vs*. AdFn and Si *vs* SiFn). ↑ Shear stress for SiFn *vs* AdFn. ↑ Cell area for AdFn *vs* SiFn At 4 hours: ↑shear stress for adsorbed Fn substrates *vs* uncoated controls (Pol vs. AdFn and Si vs. SiFn), ↑ Cell areas on Fn-coated substrates *vs* uncoated controls (Pol vs. AdFn and Si *vs* SiFn). At 24 hours: ↑ shear stress and FA density on adsorbed Fn substrates *vs* uncoated controls (Shear stress: Pol *vs* AdFn and Si *vs*. SiFn; FA density: Pol *vs*. and Si *vs* SiFn). ↑ FA density and cells for AdFn *vs* SiFn		
Anodization process used to realize TI nanotube in comparison to Ti control substrate	Human dermal fibroblasts (HDF) and human epidermal keratinocytes (HEK)	Adhesion, proliferation and viability at 1, 2 and 4 days Cells morphology, cytoskeletal reorganization and differentiation at 4 days.	↑ adhesion and proliferation of HDF on Ti nanotubes after 4 days ↓ adhesion and proliferation of HEK on Ti nanotubes after 4 days	Ti nanotube provide a favorable surface for adhesion and proliferation of HDF cells. This surface prevents HEK adhesion and	Smith, 2011

			40% increase of HDF on Ti nanotube surface coverage and a 92% decrease in HEK cell coverage *vs* control substrate. ↑ alignment of HDF cells on Ti nanotube arrays *vs* control substrate. ↑ HDF viability after 4 days on nanotubes *vs* control substrate. ↓ HEK viability on Ti nanotube *vs* control substrate. ↑ expression of vinculin and F-actin by HDF cells, while minimal expression for HEK cells. ↑ expression of collagen Ia1 and fibrillin 1 for HDF cells on Ti nanotube arrays. ↓ expression of cytokeratin 19 and laminin b3 for HEK cells on Ti nanotube *vs* control.	proliferation, restricting the downgrowth along the implanted biomaterial.	
Chitosan mixed with chitosan/poly(ethylene oxide) (PEO) at 75:25 ratio with the addition to the polymer of 0.1, 1 and 5 wt% of AgNO3. Nanofibrous membrane were post loaded with 20, 40,60 ug of CHX (chlorhexidine)	Human foreskin fibroblasts	Citotoxicity at 24 hrs Antibacterial effects with S.aureus for 20 hrs after 1,2,3 and 4 days of loading	Cytotoxicity for membranes containing ≥60 µg of CHX. No cytotoxic effect for membranes loaded with 20 µg CHX or with AgNO3. No cytotoxic for AgNO3 up to the highest concentration tested (50 µg/ml), Inhibition zone for AgNO3 of 1 and 5 wt% and for membranes	The membranes have a potential to act as an active antibacterial dressing for percutaneous device	Song, 2016

			loaded with 20 µg CHX and 60 µg CHX.		
Ti alloy (Ti6Al4V) disks with surface coatings: - uncoated polished Ti6Al4V (Pol), - Hydroxyapatite (HA) electrochemical deposited - Hydroxyapatite and fibronectin (HAFn), - Hydroxyapatite with silver (HAAg) at 10, 50 and 100 mg of AgNO3 (HAAg10, HAAg50 and HAAg100) - Hydroxyapatite with silver and fibronectin (HAAgFn10, HAAgFn50 and HAAgFn100). All surfaces were studied before and after preconditioning by immersion in fetal calf serum for 24 h (P24).	Human dermal fibroblasts (1BR3G)	Live/dead at 24 hrs Cells Metabolism at 24 hrs Biofilm formation at 24 hrs with S Aureus. Planktonic colony count at 24 hrs S Aureus.	All non-preconditioned HAAg surfaces were cytotoxic to fibroblasts *vs* to Pol, HA, and HAFn ↑ cytotoxicity for HAAg100 and HAAgFn100 *vs* HAAg50 and HAAg10. After 24 h preconditioning, all surfaces were cytocompatible. ↑ cell metabolism on HAFn *vs* Pol. ↓cell metabolism on HAAg surfaces not preconditioned *vs* Pol, HA, and HAFn surfaces. ↓ cell metabolism on HAAg100 surfaces *vs* HAAg50 and HAAg10 surfaces. No difference in cell metabolism between HAAg10, HAAg50, and HAAg100 surfaces after preconditioning and no difference between these surfaces and Pol and HA controls. ↑cell metabolism on HAFn controls than on HAAg (P24) surfaces. ↑bacteria within biofilms on HA compared to Pol and on	HAAg100 and HAAgFn100 suppressed bacterial colonization before and after preconditioning After preconditioning, all silver containing surfaces were cytocompatible and supported the growth of fibroblasts. Cell metabolism also increased after preconditioning,	Chimutengwende-Gordon, 2014

			HAFn in comparison to HA. ↓ bacterial colonization on nonpreconditioned HAAg in comparison to Pol, HA, and HAFn. Increasing the silver content increased the degree of antibacterial activity. After preconditioning, HAAg10 and HAAg50 lost their antibacterial activity compared to Pol, but fewer bacteria colonized these surfaces than HA. Reduced numbers of bacteria colonized Pol, HA, and HAFn surfaces after preconditioned while increased numbers of bacteria colonized HAAg and HAAgFn surfaces after they were preconditioned. HAAg100 maintained an antibacterial effect after preconditioning compared to Pol. ↑ antibacterial activity for HAAg100 and HAAgFn100 compared to control surfaces before and after serum-preconditioning in planktonic condition.		
Ti samples (TiAl6V4) coated with different nanometer copolymers films (Dimethyl(2-hydroxyethyl) phosphonate, 4-vinylpyridine (VP);	Human dermal fibroblasts (HDFibs)	Viability, number of attached cells onto surfaces at 24 and 72 hrs Cells morphology by SEM at 24 and 72 hrs	No significant differences in proliferation among copolymers and control Cell morphology on copolymers was comparable to	A balance between antibacterial activity and biocompatibility for HDFibs was founded in copolymer D	Callies, 2012

dimethyl(2-methacryloyloxyethyl) phosphonate (DMMEP) and vinylbenzylphosphonate (VBP)): A) VP:VBP B) VP:DMMEP C) VP:DMMEP D) VP:DMMEP prepared with free radical polymerization in comparison with titanium control		Antimicrobial activity against Staphylococcus epidermidis and Staphylococcus aureus at 1hr.	those onto titanium. Copolymer A as well as copolymer B showed a uniform colonization of bacteria on the surface, Copolymer C was more effective from antibacterial point of view while copolymer D showed a reduction up to 95% of bacteria adhesion *vs* control samples.		
Pellets of: - Fluorohydroxyapatites (FHA) - Fluorapatite (FA), - Hydroxyapatite (HA) at three different sintering temperature (1250 °C - 1050 °C -1150 °C) Ti pellet served as control	HaCaT cells (keratinocytes) and NIH 3T3 murine fibroblast cells	Adhesion study at 2 days; Immunocytochemistry for involucrin to evaluate keratinocytes differentiation Antimicrobial activity with Staphylococcus aureus for 6 hrs	HaCaT adhesion rate: Ti pellets : 92 ± 12%. HA and FHA (1050 °C) ↓ adhesion than Ti; HA (1250 °C) ↑ adhesion than Ti; FHA (1250 and 1150 °C) ↔ to HA; FA ↑adhesion *vs* other groups. NIH3T3 adhesion rate: Ti pellet: 415 ± 27%; HA and FHA (1050 °C) ↓ adhesion than Ti; HA ↑ adhesion than Ti for the other temperature; FHA (1250 and 1150 °C) ↑ adhesion than Ti; FA no differences among sintering temperature ↑expression of involucrin for FA	Results suggested the enhanced ability of FA surfaces to promote terminal differentiation of keratinocytes. Significantly more keratinocytes adhered to the FA surfaces. FHA failed to show a similar improvement in terms of keratinocyte adhesion and proliferation *vs* Ti or HA surfaces Planktonic form of *S. aureus* is not affected by the addition of fluoride, and FHA/FA.	Bennett, 2019

			at 1250 °C (86 ± 4%), followed by FA at 1150 °C (72 ± 7%), and FA sintered at 1050 °C (67 ± 4%). No significant differences in bacterial adhesion between experimental groups and Ti control		
Ti plates submitted to micro-arc oxidation (MAO) to obtain coatings with different concentration of Copper (Cu) Cu-free (CA) surfaces and Ti plates as controls	Mouse fibroblast cell line, L-929,	Cells adhesion, proliferation and viability at 1h, 1,3 and 7 days SEM at 1h, 1,3 and 7 days Biochemical analysis at 1, 3 and 7 days In vitro antibacterial tests with S. Aureus at 6, 24, 48 and 96 hrs.	↑ proliferation and viability on all surface at 7 days in the following order: Cu1 ≥ CA ≥ Cu2 ≥Cu3 ≥ Ti ≥ Cu4. Citotoxicity of Cu4 At 7 days the cells grow as layer by layer on Ti, CA, Cu1, Cu2 and Cu3 while on Cu4, the number of cells is ↓ and the morphology collapsed. ↑ amounts of Col-I and CTGF at each time point in the following order: Cu4 ≥ Cu3 ≥ Cu2 ≥ Cu1 ≥ CA ≥ Ti. At 7 d of incubation, ↑ amount of a-SMA for Ti, CA and Cu1 indicating that Cu^{2+} accelerates the fibroblasts switching to a more fibrotic phenotype and differentiating into myofibroblasts. The Cu^{2+}-doped TiO_2 surfaces inhibit the attachments of S. aureus; increasing the content of Cu the effect of anti-attachment on S. aureus is increasingly significant.	Microporous TiO_2 with an content of Cu^{2+} (e.g. Cu1) is suitable for cell adhesion and proliferation and able to inhibit S. Aureus adhesion	Zhang, 2016

Ti plates submitted to MAO and hydrothermal treatment (HT) for 1, 4, 6 and 48 hours (HT1h, HT4h, HT6h and HT48h) *vs* MAOed, TiO2 and Ti.	Mouse fibroblast cell line, L-929	Cells adhesion, proliferation and viability at 1h, 1,3 and 7 days SEM at 1h, 1,3 and 7 days Biochemical analysis at 1, 3 and 7 days In vitro antibacterial tests with S. Aureus and E.Coli at 24 h	↑ proliferation and viability on surface at 7 days in the following order: HT4h > HT1h > HT6h > HT48h > As-MAO ed TiO2 > Ti. After 3 days cells appeared spindle and communicate with their elongated finger-like pseudopodium on all surfaces. ↑ amounts of Col-I, CTGF and in α-SMA the following order: HT4h > HT1h > HT6h > As-MAOed TiO2 > HT48 ≈ Ti. The adhered numbers of bacteria ↓ on coating surfaces in comparison with Ti, especially for S. aureus.	Coatings as HT1h, HT4h could be used for percutaneous implant as increased fibroblast functions and possessed anti-bacterial ability	Zhang, 2017
Ti plates submitted to micro-arc oxidation (MAO) to obtain coatings doped with Copper (Cu) and different amount of zinc (CA - Zn0 - Zn1 - Zn2 - Zn3 - Zn4) *vs* Cu-free (CA) surface and Ti.	Mouse fibroblast cell line, L-929	Cells adhesion, proliferation and viability at 1, 3 and 7 days SEM at 1, 3 and 7 days Biochemical analysis at 1, 3 and 7 days In vitro antibacterial tests with S. Aureus at 6 and 24h.	↑ proliferation in the following order: Zn2 > Zn3 > Zn1 > Zn0 > CA > Zn4. ↑ viability on all surfaces. ↑ adhesion on Zn0–Zn3, especially on Zn2, while ↓ on Zn4. L929 appeared polygonal and spread on CA and Zn0–Zn3. ↑ synthesis at 7 d of Col I and CTGF in the following order: Zn3 > Zn2 ≈ Zn0 > Zn1 > CA. CA does not show antibacterial activity. ↓ adhesion of S. Aureus on	Doped coating with Cu and Zn0–Zn3 enhance fibroblast viability, and exert an antibacterial effect.	Zhang, 2018

			Zn0–Zn3 surfaces at 6 h and a slight increase at 24 h.		
Zirconia (Zr) plates submitted to micro-arc oxidation (MAO) and hydrothermal treatment (HT) for 4, 6, 12 and 24 hours (HT4h, HT6h, HT12h and HT24h) to realized nano-rod structures in comparison to as-MAOed, and Zr control	Mouse fibroblast cell line, L-929	Cells adhesion, proliferation and viability at 1h, 1,3 and 7 days SEM at 1h, 1,3 and 7 days	↑ proliferation in the following order: HT-24 h > as- MAOed ZrO_2 > Zr (control). HT24h surface covered with cells with dense lamellipodia and filopodia anchored to the HA nanorods	HT resulted in the formation of HA nanorods on the coating surface. This HA nanorods improve cells adhesion and proliferation.	Zhang, 2015
Ti disks treated with MAO technique to obtain a surface functionalization with Magnetic Fe_3O_4 nanoparticles (NPs) at 3 different concentration 0 (CA), 0.25 (FT1), 0.75 (FT2) and 2.25 g L^{-1} (FT3) *vs* polished titanium (pol Ti).	Mouse fibroblast cell line, L-929	Cell viability at 1, 3, and 7 days. Cells morphology at 1 and 3 days Intracellular quantification of connective tissue growth factor (CTGF) and Col-I at 3, 7 and 14 days Antibacterial test with S. aureus at 6 and 24 hours	↑ cells viability at 1 day on pol Ti and no difference among the NPs coatings. ↑ cell viability at 3 and 7 days in the following order: FT3 ≥FT2 ≥ FT1 ≥ CA ≥ pol Ti ↑ amount of Col-I and CTGF in the following order: FT3 ≥FT2 ≥ FT1 ≥ CA ≥ pol Ti Increase amount of Fe_3O_4, reduced the number of S. aureus adhered on the coating surfaces with no significant difference, Reduction of 60% adherent bacteria on FT3 in comparison with CA	The incorporation of Fe_3O_4 enhance the viability and proliferation of fibroblast	Li, 2019*
Ti disks treated with alkali-heat treatment (AHT) followed with hydrothermal treatment (HT) in order to obtain a hydroxyapatite HA nanorod and Si-HA nanorod obtained with the addition of	Mouse fibroblast cell line, L-929	Cells viability and proliferation at 1, 3 and 7 days Molecular expression of α-SMA, CTGF, TGF-β1, and Col-I at 3 and 7 days	↑ cells proliferation at 1 day in the following order: Si-HA > HA > Ti. Spherical morphology for cells at 1 day on Ti, while spread morphology was observed on	Nanorod topography and Si substitution in HA can enhance cells attachment HA nanorods especially the Si substituted	Li, 2020*

Si in the hydrothermal treatment *vs* polished titanium		Extracellular collagen quantification at 3 and 7 days	HA and especially on Si-HA. ↓ cell adhesion on HA at 3 days *vs* Si-HA and Ti ↑ gene expression on each surface in the following order: Si-HA > HA > Ti. Collagen secretion in the order: Si-HA > HA > Ti from 3 to 7 days.	improved functional expression of fibroblasts. The combined effect of Ca and Si ions and HA nanotopography enhanced cell response.	
Ethylene–vinyl alcohol copolymer (EVOH) plate coated with a liquid-phase coating process with a solution of calcium phosphate supplemented with 0, 4, 10 and 20 µg mL−1 of FGF-2.	Fibroblast like NIH3T3 cells	Cells proliferation at 72 hours	↑ cells density and dimension with F4 and F10 *vs* F0 Spindle shape and presence of pseudopodia for fibroblast cultured with F4 and F10.	Coating able to promote fibroblast proliferation	Sasaki, 2010*
Sintered porous Ti rods (Ti6AL4V ELI) with pore sizes 40 – 100 µm, and porosity 45±5%, with a nanotubular surface realized with anodization process in comparison in comparison with un modified surface	Fibroblast obtained from rabbit derma	Morphology at 5, 10 and 15 days	No differences in cell morphology *vs* unmodified titanium at 5 days. ↑ Cellular density after the 15th day of incubation with well spread fibroblasts with large bundles on nanotubular Ti No significant increase in cellular density on unmodified surface at 15 days	The anodization and the realization of a nanotubular structure increased the cellular density	Shevtsov, 2016
Silanized Ti6Al4V discs functionalized with iodinated laminin-332 in comparison with: - not silanized iodinated laminin 332 (adsorbed group); - polished titanium (control); - silanized titanium.	HaCaT keratinocytes cells	Proliferation at 24 hours Focal Adhesion detection at 24 hours Cell area quantification at 24 hours	No difference in proliferation between control, adsorbed, or L-332-Ti6Al4V discs at 24 h. ↓ of 22–25% of proliferation for silanized titanium *vs* the other surfaces Cell area of HaCat onto	Silanized surface functionalized with L332 promoted more strongly the cell adhesion to Ti6Al4V	Gordon, 2010

			silanized L332 was smaller *vs* the other surfaces. ↑ Focal adhesion expression for silanized L332 *vs* the control group (more 20%). ↓ vinculin plaques for HaCaTs on silanized control discs while ↑ plaques for adsorbed discs.		
Nanotubular Titanium realized with anodization and nanorough titanium (Ti) substrates realized with electron beam evaporation in comparison with unmodified surfaces.	Commercially available human keratinocytes	Cells adhesion at 4 hours Cells proliferation at 1, 3 and 5 days Cells morphology at 4hrs, 1,3 and 5 days	↑ cells adhesion on nanotubular and nanorough Ti *vs* unmodified Ti after 4 h. No significant difference between the nanotextured substrates ↑ cell proliferation on nanorough Ti *vs* unmodified Ti. Unmodified Ti promoted keratinocyte proliferation *vs* nanotubular Ti. ↑ cells spreading on nanotubular and nanorough Ti substrates with more extended filopodia *vs* unmodified Ti substrates.	Keratinocyte adhesion was favored by the Ti substrates with nanotextured features	Puckett, 2010
Chitosan-Polyethylene glycol (CS_PEG) membranes with incorporated three concentrations of silver (Ag) coded as silver nanocluster AgNC0.1, Ag AgNC 0.5, and Ag AgNC 1.0.	Human skin keratinocytes A341 cell lines	Cells viability at 24 hours Cell Adhesion and Proliferation at 24 hours Antibacterial activity (overnight) and growth inhibition test (24 hrs) with Escherichia coli and Staphylococcus aureus	Antibacterial activity against both bacteria for AgNCs, with increasing activity as a function of AgNCs concentration. No microbial growth for Ag1.0 Absence of cytotoxicity for CS−PEG and AgNCs. ↑ cells adhesion and	The silver contents inhibit biofilm formation and stimulate cell viability and adhesion. AgNCs impregnated membranes are promising percutaneous devices	Mishra, 2016

			proliferation on AgNCs membranes ~1.8 times higher *vs* to chitosan alone.		
Microwave plasma chemical vapor used to deposit ultrananocrystalline diamond (UNCD) thin films (150 nm) on microporous silicon nitride membranes with an array of 100 x 100 2.5 µm diameter pores with a high-density hexagonal layout and 4.5 µm pitch.	neonatal human epidermal keratinocytes	Cells viability at 24 hrs	↑ viability on the silicon nitride membranes and on UNCD-coated silicon nitride membranes *vs* coverslip control and the well control.	Potential use of the UNCD coating to improve the skin sealing	Skoog, 2012
Ti foils submitted to anodization to produce nanotube array and nanorough surface by means Temscal Electron Beam Evaporator *vs* conventional titanium surface (nano-smooth). All surfaces were functionalized with FGF-2	Keratinocytes	Cell density at 1 and 5 days	↑ cell density onto both nanostructured surfaces *vs* conventional Ti at both time points ↑ density onto nanostructured functionalized surfaces with FG2 vs no functionalized surfaces Comparable cells density among nanostructure surfaces and conventional titanium functionalized with FGF2	Immobilization of FGF-2 seems to increase keratinocyte density Nanorough and nanotubular Ti surfaces promoted keratinocyte density in comparison to nanosmooth titanium Anodization or electron beam evaporation confer nanostructured features that promote keratinocyte function (even without the use of FGF-2)	Zile, 2011a
Surgical grade ground and polished Tialloy (Ti6V4Al) coated with different concentration (5, 10, 15, 20, or 30 ug/mL) of the extracellular domain of E-cadherin (F-ECD) or with different concentration of short peptide containing fifth	Murine keratinocytes (FSK 7.1 ECACC)	Adherens junction quantification and analysis. Focal contact quantification and analysis Cell metabolism End point: 4, 12, 24, 48,	No significant differences for the 5-ECD in comparison with control substrates for the parameters 24 hours: ↑ intensity of beta-catenin between 10 and 15 ug/mL of E-cadherin and no significant	The adsorption of 15 ug/mL of the F-ECD E-cadherin significantly increases metabolic activity, cell area and attachment of murine keratinocytes in vitro.	Pendegrass, 2012b

domain of the F-ECD (5-ECD) *vs* uncoated polished disks		and 72 h	differences for higher concentrations or between uncoated and 5 ug/ml at 24 and 48 hours ↑ vinculin count with 5 ug/mL of E-cadherin *vs* uncoated controls but no significant increase for the higher concentrations at 24 and 48 hours No significant differences in cell area at 24 hours while at 48 hours cell area increased with increasing E-cadherin concentration up to 15 ug/mL. No differences in vinculin density among the concentration tested at 24 and 48 hours ↑significant increase for metabolic activity between 20 and 30 ug/mL at 24 hours while at 48 hours between 5 and 10 ug/mL Study with only 15ug/mL: ↑ b-catenin intensity on coated E-cadherin substrates *vs* uncoated. No differences in metabolic activity, vinculin count, cell area, or vinculin density at 4 hours ↑ b-catenin intensity, metabolic activity, vinculin count, cell area at 12 and 24 h on E-cadherin coated substrates *vs*		

			uncoated controls ↑ b-catenin intensity, vinculin counts and cell area on E-cadherin coated substrates *vs* uncoated controls. No difference in metabolic activity at 48 and 72 hours). ↓ Vinculin density on coated substrates at both time points but significant at 48hours		

ABBREVIATIONS:

Titanium = Ti; Poly(2-hydroxyethyl methacrylate = PHEMA; Nylon 6 = N6; Nylon12 = N12; Polycaprolactone = PCL; Poly(methyl methacrylate = PMMA; Poly(D,L-lactic acid = PDLLA; Human gingival epithelial cells = HGEs; Human gingival fibroblasts = HGFs; Alkali Heat = AH; Polydopamine = PDA; Hydroxyapatite = HA; Carboxymethyl chitosan = CMCS; Human Dermal Fibroblast = HDF; Melt electrowriting = MEW; Titania Nano-Tubes = TNT; Polished Ti = pTi; Polished = Pol; Silanized = Si;