What is claimed is:

1. A drug eluting stent, comprising at least four parts:

a stent framework;

a drug-containing layer;

a drug embedded in the drug-containing layer; and

a biocompatible base layer disposed over the stent framework and supporting the drug-containing layer,

wherein one or more parts of the stent have been designed to produce a stent that is capable of achieving a pre-designed drug release pharmacokinetic profile selected from:

(1) the drug has a pharmacokinetic profile that has Tmax and Cmax (expressed in µg of drug per g of the artery tissue after implantation into the coronary or iliac artery of either a rabbit or a pig) so that:

(a) Tmax is between 400 and 600 hr, preferably 500 hr,

(b) Cmax is between 5 and 15 µg/g, preferably 10 µg/g, and/or

(c) the drug pharmacokinetic profile overlaps with the kinetic profile for smooth muscle cell proliferation post-stent implantation and is substantially the same as that shown in FIG. 16B, preferably wherein the arterial tissue concentration at the site of stent implantation peaks between 15 and 25 days, preferably at 20 days, and then decreases to allow for vascular restoration; and

(2) the drug has a pharmacokinetic profile in the arterial tissue at the site of stent implantation substantially the same as that shown in FIG. 16A or FIG. 16B; optionally, wherein the drug is sirolimus.

2. The drug eluting stent of claim 1, wherein the drug is embedded essentially on the drug-containing layer on an abluminal side of the stent.

3. The drug eluting stent of any one of claims 1 through 2, wherein the stent framework is fabricated from a single piece of metal, wire, or tubing; preferably, wherein the metal comprises at least one of stainless steel, nitinol, tantalum, cobalt-chromium MP35N or MP20N alloys, platinum, and titanium.

4. The drug eluting stent of any one of claims 1 through 3, wherein the stent framework is fabricated from a biodegradable material, such as a metallic alloy made from magnesium, zinc or iron.
5. The drug eluting stent of any one of claims 1 through 4, wherein the drug comprises at least one of an antithrombogenic agent, an anticoagulant, an antiplatelet agent, an antineoplastic agent, an antiproliferative agent, an antibiotic, an anti-inflammatory agent, a gene therapy agent, a recombinant DNA product, a recombinant RNA product, a collagen, a collagen derivative, a protein analog, a saccharide, a saccharide derivative, an inhibitor of smooth muscle cell proliferation, a promoter of endothelial cell migration, proliferation, and/or survival, and combinations of the same; preferably, wherein the drug comprises sirolimus and/or a derivative or analog of sirolimus.
6. The drug eluting stent of claim 1, wherein the drug-containing layer has a thickness between 5 and 12 μm or 2-20 μm, preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16. 17, 18, 19, or 20 μm in either the luminal, abluminal, or both sides.
7. The drug eluting stent of claim 1, wherein the drug-containing layer is selected from the group consisting of poly(hydroxyalkanoates) (PHAs), poly(ester amides) (PEAs), poly(hydroxyalkanoate-co-ester amides), polyacrylates, polymethacrylates, polycaprolactones, poly(ethylene glycol)(PEG), poly(propylene glycol)(PPG), poly(propylene oxide) (PPO), poly(propylene fumarate) (PPF), poly(D-lactide), poly(L-lactide), poly(D,L-lactide), poly(meso-lactide), poly(L-lactide-co-meso-lactide), poly(D-lactide-co-meso-lactide), poly(D,L-lactide-co-meso-lactide), poly(D,L-lactide-co-PEG), poly(D,L-lactide-co-trimethylene carbonate), poly(lactide-co-glycolide), poly(glycolic acid-co-trimethylene carbonate), poly(trimethylene carbonate), PHA-PEG, PBT-PEG (PolyActive(R)), PEG-PPO-PEG(Pluronic(R)), and PPF-co-PEG, polycaprolactones, polyglycerol sebacate, polycarbonates, biopolyesters, polyethylene oxide, polybutylene terephalate, polydioxanones, hybrids, composites, collagen matrices with grouth modulators, proteoglycans, glycosaminoglycans, vacuum formed small intestinal submucosa, fibers, chitin, dexran and mixtures thereof; preferably, wherein the drug-containing layer is selected from tyrosine derived polycarbonates and poly(β-hydroxyalcanoate)s and derivatives thereof.

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8. The drug eluting stent of claim 1, wherein the drug-containing layer comprises a polylactide-co-glycolide 50/50 (PLGA) or Poly Butyl MethAcrylate.

9. The drug eluting stent of claim 1, wherein the biocompatible base layer comprises at least one of poly poly-butyl methacrylate, poly-N-[Tris(hydroxymethyl)-methyl]-acrylamide (poly-NTMA), Poly-dopamine, PEDOT, PTFE, PVDF-HFP, poly(styrene-b-isobutylene-b-styrene), Parylene C, PVP, PEVA, SBS, PC, or TiO2; and/or wherein the biocompatible base layer comprises an electro-grafted layer, optionally an electro-grafted polymeric layer, optionally interdigitating with the drug-containing layer; preferably, wherein: (i) the biocompatible base layer comprises an organic layer obtained by chemical grafting of phenyl diazoniums or azides; and/or (ii) the grafted layer has a thickness between 10 nm and 1000 nm, preferably between 100 nm and 200 nm.

10. The drug eluting stent of claim 9, wherein the electro-grafted polymeric layer comprises a monomer selected from the group consisting of vinylics, epoxides, and cyclic monomers undergoing ring opening polymerization and aryl diazonium salts; preferably, wherein the monomer is further selected from the group consisting of butyl methacrylate, methyl methacrylate, hydroxyethyl methacrylate, epsilon caprolactone, N-[Tris(hydroxymethyl)-methyl]-acrylamide (NTMA) and 4-nitrophenyl diazonium tetrafluoro borate.

11. A method of (i) selecting the product parameters of a drug eluting stent and/or (ii) predicting the outcome of the stent implantation at 1-year or more post-stent implantation into a human (e.g., thrombosis), comprising preparing the stent, implanting the stent into the iliac or coronary artery of a rabbit or a pig, respectively, and measuring the percentage of neointima coverage over the stent in the arterial tissue where a stent is implanted, at 30 days post-stent implantation, wherein the higher the percentage of neointima coverage over the stent at 30 days, the better the stent in terms of stent efficacy and/or safety in the human.

12. The method of claim 11, wherein the percentage of neointima coverage over the implanted stent at about 30 days/1 month is predictive of stent implantation side effects at 1-year or more post-stent implantation in a human, wherein a 80-90% neointima coverage at about 30 days/1 month is representative or predictive of low side effects at 1-year post-stent implantation in a human; preferably, wherein the percentage of neointima coverage

may be assessed by measuring strut coverage; more preferably, wherein the presence of neointima coverage may be assessed by OCT.

13. The method of claim 12, wherein a covered strut is a strut having a neointimal thickness above 0, preferably above 20, micrometers above the surface of the strut.

14. A drug-eluting stent, comprising at least four parts:

a stent framework;

a drug-containing layer;

a drug embedded in the drug-containing layer; and

a biocompatible base layer disposed over the stent framework and supporting the drug-containing layer, wherein the stent has the following characteristics in a rabbit or pig trial, after implantation in the iliac artery or coronary artery, respectively:

(a) the uptake of Evans' Blue dye by the artery in the stented zone is <40% at 45 days and <25% at 90 days;

(b) The ratio R, measured by confocal microscopy in a longitudinal cross-section of the stented zone of the stented artery, of the quantity of P120 protein to that of VE-Cadherin (R = [P120] / [VE-cad]), which characterizes the degree of co-localization of the said proteins in the scaffolded region, is higher than 70% at 45 days, and higher than 80% at 90 days; and

(c) The cell shape index I, defined as the ratio between the largest length [a] of endothelial cells observed by confocal microscopy divided by the size [b] in the direction perpendicular to said longest length (I = [a] / [b]), is larger than 2 at 45 days after implantation, and larger than 3.5 at 90 days after implantation.

15. The stent of claim 14, wherein one or more parts of the stent are designed for the stent to achieve a pre-designed drug release pharmacokinetic profile after implantation into the rabbit or pig, selected from:

(1) the drug as a pharmacokinetic profile having Tmax and Cmax (expressed in µg of drug per g of the artery tissue after implantation) so that:

(a) Tmax is between 400 and 600 hr, preferably 500 hr,

(b) Cmax is between 5 and 15 µg/g, preferably 10 µg/g, and/or

(c) the drug has a pharmacokinetic profile that overlaps with the kinetic profile for smooth muscle cell proliferation post-stent implantation and is substantially the same as that shown in FIG. 16B, preferably wherein the arterial tissue concentration at the site of stent implantation peaks between 15 and 25 days, preferably at 20 days, and then decreases to allow for vascular restoration; and

(2) the drug has a pharmacokinetic profile in the arterial tissue at the site of stent implantation that is substantially the same as that shown in FIG. 16A or FIG. 16B, optionally, wherein the drug is sirolimus.

16. A method of preparing a drug-eluting stent, wherein the drug-eluting stent achieves between 80% and 100% neointima strut coverage between day 20 and day 60 post-stent implantation in an animal model, more preferably, about 30 days post-stent implantation; and preferably after implantation into the coronary or iliac artery of either a rabbit or a pig, respectively;

wherein the stent comprises at least four parts:

a stent framework;

a drug-containing layer;

a drug embedded in the drug-containing layer; and

a biocompatible base layer disposed over the stent framework and supporting the drug-containing layer,

the method comprising producing the stent using said parts, wherein one or more of said four parts have been designed in order for the stent to achieve a pre-designed drug release pharmacokinetic profile selected from:

(1) the drug has a pharmacokinetic profile that has Tmax and Cmax (expressed in µg/g of drug per g of the artery tissue after implantation into the coronary or iliac artery of either a rabbit or a pig, respectively) so that:

(a) Tmax is between 400 and 600 hr, preferably 500 hr;

(b) Cmax is between 5 and 15 µg/g, preferably 10 µg/g; and/or

(c) the drug pharmacokinetic profile overlaps with the kinetic profile for smooth muscle cell proliferation post-stent implantation and is substantially the same as that shown in FIG. 16B, preferably wherein the arterial tissue concentration

at the site of stent implantation peaks between 15 and 25 days, preferably at 20 days, and then decreases to allow for vascular restoration; and

(2) the drug has a pharmacokinetic profile in the arterial tissue at the site of stent implantation substantially the same as that shown in FIG. 16A or FIG. 16B; optionally, wherein the drug is sirolimus.

17. A method of preparing a drug-eluting stent, wherein the drug-eluting stent achieves between 80% and 100% neointima strut coverage between day 20 and day 60 post-stent implantation in an animal model, more preferably, about 30 days post-stent implantation; and preferably in a rabbit or pig trial, after implantation in the iliac artery or coronary artery;

wherein the stent comprises at least four parts:

a stent framework;

a drug-containing layer;

a drug embedded in the drug-containing layer; and

a biocompatible base layer disposed over the stent framework and supporting the drug-containing layer,

the method comprising producing the stent using said parts, wherein one or more of said four parts have been designed in order for the stent to have the following characteristics in a rabbit or pig trial, after implantation in the iliac artery or coronary artery, respectively:

(a) an uptake of Evans' Blue dye by the artery in the stented zone is <40% at 45 days and <25% at 90 days;

(b) a ratio R, measured by confocal microscopy in a longitudinal cross-section of the stented zone of the stented artery, of the quantity of P120 protein to that of VE-Cadherin (R = [P120] / [VE-cad]), which characterizes the degree of co-localization of the said proteins in the scaffolded region, is higher than 70% at 45 days, and higher than 80% at 90 days; and

(c) a cell shape index I, defined as the ratio between the largest length [a] of endothelial cells observed by confocal microscopy divided by the size [b] in the direction perpendicular to said longest length (I = [a] / [b]), is larger than 2 at 45 days after implantation, and larger than 3.5 at 90 days after implantation.

18. The method of any one of claims 16 and 17, wherein the drug is embedded essentially on the drug-containing layer on an abluminal side of the stent.
19. The method of any one of claims 16 to 18, wherein the stent framework is fabricated from a single piece of metal, wire, or tubing; preferably, wherein the metal comprises at least one of stainless steel, nitinol, tantalum, cobalt-chromium MP35N or MP20N alloys, platinum, and titanium.
20. The method of any one of claims 16 to 19, wherein the stent framework is fabricated from a biodegradable material, such as a metallic alloy made from magnesium, zinc or iron.
21. The method of any one of claims 16 to 20, wherein the drug comprises at least one of an antithrombogenic agent, an anticoagulant, an antiplatelet agent, an antineoplastic agent, an antiproliferative agent, an antibiotic, an anti-inflammatory agent, a gene therapy agent, a recombinant DNA product, a recombinant RNA product, a collagen, a collagen derivative, a protein analog, a saccharide, a saccharide derivative, an inhibitor of smooth muscle cell proliferation, a promoter of endothelial cell migration, proliferation, and/or survival, and combinations of the same; preferably, wherein the drug comprises sirolimus and/or a derivative or analog of sirolimus.
22. The method of any one of claims 16 to 21, wherein the drug-containing layer has a thickness between 5 and 12 μm or 2-20 μm, preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16. 17, 18, 19, or 20 μm in either the luminal, abluminal, or both sides.
23. The method of any one of claims 16 to 22, wherein the drug-containing layer is selected from the group consisting of poly(hydroxyalkanoates) (PHAs), poly(ester amides) (PEAs), poly(hydroxyalkanoate-co-ester amides), polyacrylates, polymethacrylates, polycaprolactones, poly(ethylene glycol)(PEG), poly(propylene glycol)(PPG), poly(propylene oxide) (PPO), poly(propylene fumarate) (PPF), poly(D-lactide), poly(L-lactide), poly(D,L-lactide), poly(meso-lactide), poly(L-lactide-co-meso-lactide), poly(D-lactide-co-meso-lactide), poly(D,L-lactide-co-meso-lactide), poly(D,L-lactide-co-PEG), poly(D,L-lactide-co-trimethylene carbonate), poly(lactide-co-glycolide), poly(glycolic acid-co-trimethylene carbonate), poly(trimethylene carbonate), PHA-PEG, PBT-PEG (PolyActive(R)), PEG-PPO-PEG(Pluronic(R)), and PPF-co-PEG, polycaprolactones, polyglycerol sebacate, polycarbonates, biopolyesters, polyethylene oxide, polybutylene

terephalate, polydioxanones, hybrids, composites, collagen matrices with grouth modulators, proteoglycans, glycosaminoglycans, vacuum formed small intestinal submucosa, fibers, chitin, dexran and mixtures thereof; preferably, wherein the drug-containing layer is selected from tyrosine derived polycarbonates and poly(β-hydroxyalcanoate)s and derivatives thereof.

24. The method of any one of claims 16 to 23, wherein the drug-containing layer comprises a polylactide-co-glycolide 50/50 (PLGA) or Poly Butyl MethAcrylate.

25. The method of any one of claims 16 to 24, wherein the biocompatible base layer comprises at least one of poly poly-butyl methacrylate, poly-N-[Tris(hydroxymethyl)-methyl]-acrylamide (poly-NTMA), Poly-dopamine, PEDOT, PTFE, PVDF-HFP, poly(styrene-b-isobutylene-b-styrene), Parylene C, PVP, PEVA, SBS, PC, or TiO2; and/or wherein the biocompatible base layer comprises an electro-grafted layer, optionally an electro-grafted polymeric layer, optionally interdigitating with the drug-containing layer; preferably, wherein: (i) the biocompatible base layer comprises an organic layer obtained by chemical grafting of phenyl diazoniums or azides; and/or (ii) the grafted layer has a thickness between 10 nm and 1000 nm, preferably between 100 nm and 200 nm.

26. The method of any one of claims 16 to 25, wherein the electro-grafted polymeric layer comprises a monomer selected from the group consisting of vinylics, epoxides, and cyclic monomers undergoing ring opening polymerization and aryl diazonium salts; preferably, wherein the monomer is further selected from the group consisting of butyl methacrylate, methyl methacrylate, hydroxyethyl methacrylate, epsilon caprolactone, N-[Tris(hydroxymethyl)-methyl]-acrylamide (NTMA) and 4-nitrophenyl diazonium tetrafluoro borate.