Hans Journal of Nanotechnology 纳米技术, 2021, 11(4), 278-287
Published Online November 2021 in Hans. http://www.hanspub.org/journal/nat
https://doi.org/10.12677/nat.2021.114030

关于导电材料在组织工程中应用的研究

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收稿日期：2021年9月24日；录用日期：2021年10月25日；发布日期：2021年11月4日

摘要

组织工程学一直致力于将生物细胞与材料相结合，体外或体内构建器官组织用于修复人类身体的损伤。随着研究的不断深入，支架材料也不断地仿生化、功能化，能够通过改善细胞的活性来修复或调节功能受损的组织。研究显示细胞活动与细胞内信号传导多以生物电信号的形式进行，因而导电材料可以赋予损伤组织更加良好的生物传感环境，有助于引导细胞在损伤部位的行为，包括迁移、粘附、增殖和分化。从聚合物到复合材料，再到陶瓷甚至金属，已经有各种类型的导电材料被引入组织工程中，根据其导电性能也可划分为导电与半导电。本综述旨在重点介绍并总结那些应用于组织工程中的导电生物材料的研究进展。

关键词

组织工程，导电材料，生物相容性，聚合物

Research on the Application of Conductive Materials in Tissue Engineering

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Received: Sep. 24th, 2021; accepted: Oct. 25th, 2021; published: Nov. 4th, 2021

Abstract

Tissue engineering has been committed to combining biological cells and materials to construct organs and tissues *in vitro* or *in vivo* to repair human body damage. With the deepening of research, scaffold materials are constantly biomimetic and functionalized, and can repair or mediate damaged tissues by improving cell activity. Studies have shown that cell activities and

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文章引用: 徐志新, 赵亚红, 杨宇民. 关于导电材料在组织工程中应用的研究[J]. 纳米技术, 2021, 11(4): 278-287.
DOI: 10.12677/nat.2021.114030

intracellular signal transduction are mostly carried out in the form of bioelectrical signals. Therefore, conductive materials can give damaged tissues a better biosensing environment and help guide cell behavior at the damaged site, including migration, adhesion, proliferation and differentiation. From polymers to composite materials, to ceramics and even metals, various types of conductive materials have been introduced into tissue engineering. According to their conductive properties, they can also be divided into conductive and semi-conductive. This review aims to introduce and summarize the research progress of conductive biomaterials used in tissue engineering.

Keywords

Tissue Engineering, Conductive Materials, Biocompatibility, Polymers

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1. 引言

研究显示，用于治疗器官的衰竭和组织损伤的费用大约可占美国医疗费用的一半，外科手术次数可达每年 8,000,000 而住院治疗天数可达每年 40~9000 万，平均每十五分钟就可能有一人被列入等待器官移植的名单[1] [2] [3] [4] [5]。由于器官移植需求量日益增加，而器官供给又明显不足，只有不足一半的患者能得到救治。而组织工程的兴起与发展正好是这些患者的福音，它通过将细胞工程学原理与材料学相结合进行人工组织设计以缓解器官供给短缺而带来的灾害。目前组织工程技术已被广泛应用于各种类型的组织和器官修复中，比如皮肤、心脏、神经、肌肉、软骨、骨骼和角膜等[6] [7] [8] [9]。随着研究的不断深入，人们发现功能化的生物材料能够在组织修复的过程中发挥出关键作用。它们不仅能作为细胞粘附的基质，还可以增强材料对所接种细胞的调节作用，并进一步调控细胞的生理活动，如细胞增殖和分化，甚至引导新组织的生长[10] [11]。

自从 20 世纪 60 年代 Bassett 等人定义了电诱导对组织生长的影响以来，人们又验证出机电刺激能够对骨骼的生长起刺激作用[12]。还有研究表明，在体外施加生理直流电场(1~10 V/cm)或交流电流(10~100 mA)时，能够通过干扰多种细胞的迁移、排列和细胞骨架的组织来控制细胞的行为，并能够促进神经细胞中的神经突触生长、分化，胶原蛋白生成，还能促进成骨细胞的钙化[13] [14]。因此，越来越多的研究人员将目光聚焦于具有导电性能的生物材料的开发与改进。近年来，碳纳米管、石墨烯以及金属颗粒(如金纳米颗粒)的导电生物材料由于其优异的导电性能和抗拉强度而在生物传感器和骨组织工程中得到广泛研究[15]-[22]。同时导电聚合物(CPS)作为新一代有机材料，不仅表现出类似于金属和无机半导体的电学以及光学特性，同时它们还拥有易于合成和加工灵活的特点，也受到了研究者的青睐[23] [24] [25] [26] [27]。上述这些导电材料不仅具有一定的生物相容性，还能促进细胞生理活动，包括细胞的迁移、粘附、增殖、分化并且能够促进聚合物与组织界面处活性蛋白因子的分泌[28] [29] [30] [31]。然而，这些导电材料也存在一些问题，比如导电聚合物(CPS)的生物降解缓慢所产生的体内长期毒性与炎症反应，同时还会带来二次手术的负担；导电复合材料中导电粒子分布不均从而限制了其有效地应用等。为了克服这些问题，研究人员正在不断地改进各种导电材料的制备方法。本综述将讨论作为用于组织工程应用的生物活性导电材料，总结其研究进展。

2. 导电聚合物及其复合材料

2.1. 聚吡咯及其复合材料

聚吡咯(PPy)是一种共轭聚合物，它具有特殊的电子特性因而具有良好的导电性。在生物医学工程的应用当中，它通常是以掺入其他阴离子后以电化学的方式产生，从而用于制备生物材料。1958 年 Natta 等人合成了聚乙炔，随后 Dall'olio 等人在聚乙炔的基础上掺杂卤素发现了另一种化合物聚吡咯(PPy) [32]。作为导电聚合物中最常见的选择，聚吡咯(PPy)具有高导电性，一定的柔韧性，适当的生物相容性，能够进行离子交换和表面改性，耐高温，并且可以支持细胞活性的特征[33] [34]。尤其在对细胞功能的有效性方面经常被研究。2004 年，王等人对电化学制备的 PPy 的生物相容性进行了全面的评估。他们将 PPy 粉末的浸提液应用于细胞培养和动物模型发现浸提液对细胞培养物和测试动物没有不利影响。此外，与空白玻片相比，电化学聚合的 PPy 上培养的施万细胞生长更好。该报告还显示了 PPy 在硅胶管内表面的新型电化学沉积，用于弥合大鼠坐骨神经中产生的间隙也具有良好的修复效果[35]。

与其它导电聚合物一样，聚吡咯(PPy)具有相当大的脆性，因此用纯聚吡咯制造导电聚合物薄膜非常困难。因此，研究人员将 PPy 与其他可降解的聚合物混合制备出了聚吡咯复合材料目前已被广泛用作组织工程的导电生物材料。当前常见的用于混合的材料包括 PLA、PLGA、PCL、壳聚糖和丝素蛋白在内的各种合成或天然聚合物[30] [36] [37]。Jan Lukášek 等将聚[6-(吡咯-3-基)己酸] (PPyHA)层沉积到聚己内酯(PCL)上，再将 *β*-环糊精(*β*-CD)固定在修饰有 PPyHA 的 PCL 上，制备了用于组织工程支架的环糊精－聚吡咯涂层，生物体外实验表明，该复合 PCL-PPyHA-CD 材料不仅具有生物相容性，而且大大改善了细胞与材料的相互作用[38]。目前聚吡咯及其衍生物已在人工肌肉、生物传感器、药物输送系统、固定化酶载体和组织工程方面得到了广泛应用。

2.2. 聚噻吩及其衍生物

与聚吡咯(PPy)一样，聚噻吩(PTh)及其衍生物可以通过化学氧化聚合和电化学方法合成。但不同于聚吡咯(PPy)的是，聚噻吩(PTh)是一类通过化学修饰后所具有不同性质的导电聚合物(CPs)。以噻吩、三噻吩和联噻吩单体分子作为母体，掺杂修饰各种不同的官能基团能够得到各种不同性能的聚噻吩衍生物，来满足各种应用的需求[39]。由于单体分子的多样性，聚噻吩(PTH)相较于聚吡咯(PPy)能够在更加广泛的条件下进行官能化，因此在某些情况下，聚噻吩(PTH)比其他导电聚合物(CPs)更方便[40]。

自 20 世纪 80 年代人们发现聚噻吩(PTh)以来，其有价值的衍生物不断地被引入组织工程当中。目前已经制备出多种改性的噻吩以满足不同的需要。其中聚(3,4-亚乙二氧基噻吩) (PEDOT)被认为能够替代聚吡咯(PPy)，成为能更广泛使用的导电材料，因为它具有更高的抗氧化性和更好的导电性[41]。高比表面积和独特的结构使得 PEDOT 具有较低的阻抗，加上良好的生物相容性，这让它在生物电极涂层中的应用更加广泛。杜展宏等将 EDOT 单体溶解在双(三氟甲基磺酰基)酰亚胺(EMIIM)中后进行聚合制备了聚(3,4-亚乙基二氧噻吩)－离子液体(PEDOT-IL)涂层，神经细胞培养显示 PEDOT-IL 聚合物在神经微电极表面的电化学沉积可以通过降低电阻抗大大提高神经记录性能和刺激，这种聚合物的纳米结构以及低毒性和抗神经胶质细胞污染的能力在神经界面和神经组织工程领域具有巨大的应用潜力[42]。杨伯光等使用已二酸酰肼作为交联剂交联海藻酸盐(Alg)网络，并在海藻酸盐基质中原位合成 PEDOT，制备了 PEDOT/Alg 支架，实验结果表明材料克服了纯海藻酸盐支架的脆性，并且具有优良的导电性和蛋白质吸收能力，能够支持棕色脂肪干细胞的附着与增殖[43]。

2.3. 聚苯胺及其复合材料

聚苯胺(PANI)是一种带有苯环结构的导电聚合物，由单体分子苯胺以化学或电化学聚合而成[44]。

1826 年，德国化学家 Otto Unverdorben 通过热解蒸馏靛蓝首次制得苯胺(aniline)。1840 年，Fdtzsche 从靛蓝中得到无色油状的苯胺以及苯胺的低聚物，将其命名为 aniline。但由于当时科学发展的限制，人们对高分子的本质缺乏足够的认知，聚苯胺的研究也一直止步于此。1987 年，Alan G Mac Diarmid [45]提出了苯结构单元和醌结构单元共存的 PANI 结构模型，该结构模型得到了科学界的广泛认可。由于其具有特殊的电学、光学性质，经掺杂后可具有导电性及电化学性能，经一定处理后，能够制得各种具有特殊功能的设备和材料，常用于制备导电纤维、超级电容器、可充电电池和燃料电池等。后来人们发现该聚合物还具有其他优异的特性，包括合成简单、结构形式多样、热稳定性强、环境稳定性好、一定的生物相容性、原料易获取、成本低，这使得聚苯胺及其衍生物在组织工程的导电材料领域中开始占得一席之地。还有研究证明，PANI 具有从环境中清除潜在自由基的效力，这使其有望用作缓解高氧化应激的药物[46] [47] [48] [49]。

同聚吡咯(PPy)一样，聚苯胺(PANI)可由电化学聚合，并同时掺杂各种离子或其他分子制成薄膜状，这类导电聚合物都存在固有的脆性以及不可生物降解性，为适应组织工程与生物材料的需求，人们对聚苯胺的研究探索一直没有停止。在对不同聚合度的聚苯胺进行研究的过程中，人们发现聚苯胺的低聚物即低聚苯胺与其高分子量的同类物质相比，不仅具有更低的体内异物反应，还更具有良好的导电性。另外，人们发现聚合过程中掺杂剂的种类也会影响其生物相容性[50] [51]。于是许多研究通过将低聚苯胺与具有生物可降解链段的材料(如酯键)、可快速降解聚合物(如聚乳酸)或是天然聚合物相结合来制备低毒性的生物可降解材料。例如丁华等人开发了柔性并具有生物衍生特性的肝素基导电支架材料。他们首次制备形成了可光交联的肝素－甲基丙烯酸酯水凝胶。然后将水凝胶作为模板来控制 PANI 原位聚合过程中的掺杂及其微观结构的形成。水凝胶显示出了混合电子/离子电导率和超柔性的机械性能，并在 1 kHz 下显示阻抗低至 Z = 4.17 Ω [52]。Petr Humpolíček 等将苯胺在冷冻聚乙烯醇溶液中聚合制备出一种新的独特形式的聚苯胺冷冻凝胶，该材料结合了聚苯胺固有的导电性和水凝胶的材料特性，并具有良好的生物相容性，可广泛应用于生物传感或再生医学，主要用于电激发组织的组织工程[53]。鉴于胺基和醛基在生理条件下便可以发生席夫碱反应，聚苯胺在制备可注射的导电水凝胶方面还拥有着非常广泛的研究前景。

3. 传统电子无机与金属材料

3.1. 硅

硅作为地壳上第二丰富的元素，常以硅酸盐或二氧化硅的形式广泛存在于岩石、砂砾、尘土之中。自从 1787 年，拉瓦锡首次在岩石中发现硅以来，对于这种元素的研究便一直进行。由于高度精炼的硅及其电介质(SiO_2, Si_3N_4)被证明具有生物相容性和机械稳定性，以及易于修饰的表面特性和化学性质目前已被广泛用于生物医学应用[54] [55] [56]。与其它导电材料不同的是，硅的导电性介于导体与绝缘体之间，属于半导体，其导电率与温度有很大的关系。通过阳极蚀刻或者化学蚀刻方法[57]制备的硅纳米线(SiNW)具有特殊的可调节的导电性以及生物可降解性，这使得纳米硅材料在作为生物活性材料方面焕发出新的生机[58] [59]。

3.2. 碳

碳作为自然界的一种元素，很早就为人类所知晓。自然产生的碳的同素异形体源于碳原子之间不同的共价结合方式。正是由于不同的共价结合赋予了这些同素异形体不同的空间结构，也导致它们拥有不同的性质。目前，碳纳米材料(CNS)从零维(0-D)到三维(3D)的各种同素异形体包括石墨烯(GR)、碳纳米纤维(CNF)、碳纳米管(CNT)、富勒烯(C60)等由于其出色的电化学活性、优良的导电率、一定的生物相容性已被应用于不同领域，如纳米电子学与高频电子学[60] [61]、治疗诊断学[62]、生物化学传感器[63] [64]

还有能量存储于转换等[65] [66]。

石墨烯是由sp2键合的碳原子组成的单原子厚的蜂窝状晶格平面，自2004年首次以机械剥离的方法获得单层石墨烯以来[67]，便激发了人们对其研究的强烈兴趣。由于具有优异的导热和导电性，加上良好的生物相容性，石墨烯不仅可以用于电子仪器，还非常适用于电化学生物传感器。研究表明，在聚合物中加入石墨烯可以提高原始纳米复合材料的电、机械和热学性能[68]。还有研究表明，含有石墨烯的薄膜和水凝胶具有很高的面内刚度，可以作为一种生物相容性和可移植的基质用于干细胞培养[69] [70]。Sepehr Talebian等将石墨烯纳米片与海藻酸盐共混，通过湿纺技术制备了石墨烯纳米复合纤维，实验结果显示该复合纤维具有良好的机械性能，热稳定性，优异的导电性能以及高水平的生物相容性[71]。本课题组也开发了基于氧化石墨烯的丝素蛋白/聚乙二醇二丙烯酸酯导电水凝胶。以化学键合的方式将丝素蛋白与氧化石墨烯结合，添加聚乙二醇二丙烯酸酯改善力学性能，实验结果表明该水凝胶具有高效的导电性能以及良好的生物相容性。

碳纳米管(CNT)是一种由碳原子通过sp2键相互键合而成的空心纳米结构，可以理解为卷曲成管状的石墨烯片，由Lijima于1991年首次发现[72]。碳纳米管可分为两大类：单壁碳纳米管(SWCNTs)和多壁碳纳米管(MWCNTs)。而碳纳米纤维(CNF)虽然具有与碳纳米管相似的圆柱形纳米结构、机械强度和电学性能[73]，但它是由石墨烯薄片以各种方式堆积(例如，板状、带状和人字形)而成[74]。由于具有优异的电化学性能与机械强度，CNTs和CNFs常被应用于制备仿生支架。Sanjib Bhattacharyya等人将单壁碳纳米管与透明质酸以二乙烯基砜交联制备了一种杂化水凝胶，实验结果显示该纳米复合材料具有独特的拓扑结构与动态力学性能[75]。然而，碳纳米管与碳纳米纤维的生物相容性目前还存在一些争议，不少研究显示碳纳米管具有细胞毒性作用[76] [77] [78]，目前，碳纳米管的活性分子功能化以增加其生物相容性正成为其新的研究方向。

3.3. 金纳米粒子

通过共混的方法向非导电材料中掺入导电粒子是制备导电材料的一种常见的方法。金属纳米粒子由于其天生优良的导电性，往往成为人们的首选。然而作为组织工程所需的生物材料，其生物相容性是必须要考虑的。由于纳米颗粒的普遍效应，与金属粒子接触的细胞必然经历吞噬的过程，这会导致细胞内金属粒子的聚集，这就可能产生细胞毒性与组织炎症反应。因此，低毒、低免疫原性也是组织工程中金属粒子的必然要求。金纳米粒子(AuNPs)也称为胶体金，是亚微米级金属颗粒在流体中的悬浮液，直径在3到200 nm之间。AuNPs因其特殊的特性而受到越来越多的关注，例如非凡的光学和电子特性、高稳定性和生物相容性、可控的形态和分散尺寸以及便易的表面功能化[79]。K. D. McKeon-Fischer和J. W. Freeman将聚乳酸(PLLA)与AuNPs共混，通过静电纺丝技术制备了生物可降解的纳米纤维支架，实验结果表明该纳米纤维支架具有良好的导电性，可降解性与生物相容性[80]。

4. 结论与展望

随着组织工程与生物材料研究的不断进步，同时也为了适应各种不同的条件需求，生物功能化的支架材料也越来越多地被研究与应用。导电材料由于其具有引导细胞行为以及传导生物电信号的特性而拥有着广泛的研究前景。其中导电聚合物的最大优势在于其广泛的多功能性，而掺杂剂起到了关键作用，掺杂剂的选择能够定义聚合物的特性并使其功能化以适用于特定需求。另外选择以化学或电化学合成，添加何种其它聚合物，制备薄膜、电纺纤维还是水凝胶，这些选择因素都能够对最终产物进行一定的调控，这种条件是其它材料无法提供的。当然，CPS在组织工程中的应用也存在一定的障碍。现有体系的根本障碍是聚合物–细胞相互作用较差，细胞相互作用位点缺失，疏水性、溶解性和加工性差，以及不

可控的机械特性等，这限制了导电聚合物在生物医学中的进一步应用。相较于导电聚合物，传统导电材料就具有更高效稳定的导电性与更强的抗拉机械强度，因而在骨组织工程与生物传感器方向具有更广阔的前景。但相对地，传统导电材料可修饰性有限(比如石墨烯，金纳米粒子等)导致其功能化方面存在短板，且细胞毒性方面存在些争议(如碳纳米管)，尚未有具体的体内临床数据。为了解决导电材料目前存在的问题，人们开始尝试将导电聚合物与传统导电材料结合，制备双体系或者多体系的导电材料网络，优化导电与机械性能；引入细胞外基质(ECM)，负载活性蛋白或生长因子，进一步实现组织特异性功能化并提高生物相容性，这些研究探索正在不断地取得进展。与此同时，新的研究问题也不断地产生，比如如何准确构建导电材料内部特定的空间结构？如何实时监控局部电生理活动与细胞微环境？这些可能会成为未来导电材料的研究热点。

参考文献

[1] Karp, J.M. and Langer, R. (2007) Development and Therapeutic Applications of Advanced Biomaterials. *Current Opinion in Biotechnology*, **18**, 454-459. https://doi.org/10.1016/j.copbio.2007.09.008

[2] Smith, L.A., Liu, X. and Ma, P.X. (2008) Tissue Engineering with Nano-Fibrous Scaffolds. *Soft Matter*, **4**, 2144-2149. https://doi.org/10.1039/b807088c

[3] Liu, Y., Lim, J. and Teoh, S.-H. (2013) Review: Development of Clinically Relevant Scaffolds for Vascularised Bone Tissue Engineering. *Biotechnology Advances*, **31**, 688-705. https://doi.org/10.1016/j.biotechadv.2012.10.003

[4] Farokhi, M., Mottaghitalab, F., Samani, S., Shokrgozar, M.A., Kundu, S.C., Reis, R.L., Fattahi, Y. and Kaplan, D.L. (2018) Silk Fibroin/Hydroxyapatite Composites for Bone Tissue Engineering. *Biotechnology Advances*, **36**, 68-91. https://doi.org/10.1016/j.biotechadv.2017.10.001

[5] Nilforoushzadeh, M.A., Zare, M., Zarrintaj, P, Alizadeh, E., Taghiabadi, E., Heidari-Kharaji, M., Amirkhani, M.A., Saeb, M.R. and Mozafari, M. (2018) Engineering the Niche for Hair Regeneration—A Critical Review. *Nanomedicine*: *Nanotechnology*, *Biology and Medicine*, **15**, 70-85. https://doi.org/10.1016/j.nano.2018.08.012

[6] Sefat, F., Youseffi, M., Khaghani, S.A., Soon, C.F. and Javid, F. (2016) Effect of Transforming Growth Factor-β3 on Mono and Multilayer Chondrocytes. *Cytokine*, **83**, 118-126. https://doi.org/10.1016/j.cyto.2016.04.008

[7] Zarrintaj, P., Bakhshandeh, B., Saeb, M.R., Sefat, F., Rezaeian, I., Ganjali, M.R., Ramakrishna, S. and Mozafari, M. (2018) Oligoaniline-Based Conductive Biomaterials for Tissue Engineering. *Acta Biomaterialia*, **72**, 16-34. https://doi.org/10.1016/j.actbio.2018.03.042

[8] Zarrintaj, P., Ahmadi, Z., Saeb, M.R. and Mozafari, M. (2018) Poloxamer-Based Stimuli-Responsive Biomaterials. *Materials Today*: *Proceedings*, **5**, 15516-15523. https://doi.org/10.1016/j.matpr.2018.04.158

[9] Farokhi, M., Mottaghitalab, F., Fatahi, Y., Saeb, M.R., Zarrintaj, P., Kundu, S.C. and Khademhosseini, A. (2019) Silk Fibroin Scaffolds for Common Cartilage Injuries: Possibilities for Future Clinical Applications. *European Polymer Journal*, **115**, 251-267. https://doi.org/10.1016/j.eurpolymj.2019.03.035

[10] Sukmana, I. (2012) Bioactive Polymer Scaffold for Fabrication of Vascularized Engineering Tissue. *Journal of Artificial Organs*, **15**, 215-224. https://doi.org/10.1007/s10047-012-0644-6

[11] Guo, B.L., Finne-Wistrand, A. and Albertsson, A.C. (2011) Versatile Functionalization of Polyester Hydrogels with Electroactive Aniline Oligomers. *Journal of Polymer Science Part A*: *Polymer Chemistry*, **49**, 2097-2105. https://doi.org/10.1002/pola.24643

[12] Bassett, C.A.L. and Becker, R.O. (1962) Generation of Electric Potentials by Bone in Response to Mechanical Stress. *Science*, **137**, 1063-1064. https://doi.org/10.1126/science.137.3535.1063

[13] Ning, C., Zhou, Z., Tan, G., Zhu, Y. and Mao, C. (2018) Electroactive Polymers for Tissue Regeneration: Developments and Perspectives. *Progress in Polymer Science*, **81**, 144-162. https://doi.org/10.1016/j.progpolymsci.2018.01.001

[14] Leppik, L., Zhihua, H., Mobini, S., Parameswaran, V.T., Eischen-Loges, M., Slavici, A., Helbing, J., Pindur, L., Oliveira, K.M. and Bhavsar, M.B. (2018) Combining Electrical Stimulation and Tissue Engineering to Treat Large Bone-defects in a Rat Model. *Scientific Reports*, **8**, Article No. 6307. https://doi.org/10.1038/s41598-018-24892-0

[15] Hopley, E.L., Salmasi, S., Kalaskar, D.M. and Seifalian, A.M. (2014) Carbon Nanotubes Leading the Way Forward in New Generation 3D Tissue Engineering. *Biotechnology Advances*, **32**, 1000-1014. https://doi.org/10.1016/j.biotechadv.2014.05.003

[16] Goenka, S., Sant, V. and Sant, S. (2014) Graphene-Based Nanomaterials for Drug Delivery and Tissue Engineering.

Journal of Controlled Release, **173**, 75-88. https://doi.org/10.1016/j.jconrel.2013.10.017

[17] Fan, Z.J., Wang, J.Q., Wang, Z.F., Ran, H.Q., Li, Y., Niu, L.Y., Gong, P.W., Liu, B. and Yang, S.R. (2014) One-Pot Synthesis of Graphene/Hydroxyapatite Nanorod Composite for Tissue Engineering. *Carbon*, **66**, 407-416. https://doi.org/10.1016/j.carbon.2013.09.016

[18] Abarrategi, A., Gutierrez, M.C., Moreno-Vicente, C., Hortiguela, M.J., Ramos, V., Lopez-Lacomba, J.L., Ferrer, M.L. and del Monte, F. (2008) Multiwall Carbon Nanotube Scaffolds for Tissue Engineering Purposes. *Biomaterials*, **29**, 94-102. https://doi.org/10.1016/j.biomaterials.2007.09.021

[19] Harrison, B.S. and Atala, A. (2007) Carbon Nanotube Applications for Tissue Engineering. *Biomaterials*, **28**, 344-353. https://doi.org/10.1016/j.biomaterials.2006.07.044

[20] Nair, R.S., Ameer, J.M., Alison, M.R. and Anilkumar, T.V. (2017) A Gold Nanoparticle Coated Porcine Cholecyst-Derived Bioscaffold for cardiac Tissue Engineering. *Colloids and Surfaces B*: *Biointerfaces*, **157**, 130-137. https://doi.org/10.1016/j.colsurfb.2017.05.056

[21] Shevach, M., Fleischer, S., Shapira, A. and Dvir, T. (2014) Gold Nanoparticle-Decellularized Matrix Hybrids for Cardiac Tissue Engineering. *Nano Letters*, **14**, 5792-5796. https://doi.org/10.1021/nl502673m

[22] Shevach, M., Maoz, B.M., Feiner, R., Shapira, A. and Dvir, T. (2013) Nanoengineering Gold Particle Composite Fibers for Cardiac Tissue Engineering. *Journal of Materials Chemistry B*, **1**, 5210-5217. https://doi.org/10.1039/c3tb20584c

[23] Bredas, J.L. and Street, G.B. (1985) Polarons, Bipolarons, and Solitons in Conducting Polymers. *Accounts of Chemical Research*, **18**, 309-315. https://doi.org/10.1021/ar00118a005

[24] MacDiarmid, A., Chiang, J., Richter, A. and Epstein, A.J. (1987) Polyaniline: A New Concept in Conducting Polymers. *Synthetic Metals*, **18**, 285-290. https://doi.org/10.1016/0379-6779(87)90893-9

[25] MacDiarmid, A.G. (2001) “Synthetic Metals”: A Novel Role for Organic Polymers (Nobel Lecture). *Angewandte Chemie International Edition*, **40**, 2581-2590. https://doi.org/10.1002/1521-3773(20010716)40:14%3C2581::AID-ANIE2581%3E3.0.CO;2-2

[26] Ouyang, L., Jafari, M.J., Cai, W., Aguirre, L.E., Wang, C., Ederth, T. and Inganäs, O. (2018) The Contraction of PEDOT Films Formed on a Macromolecular Liquid-Like Surface. *Journal of Materials Chemistry C*, **6**, 654-660. https://doi.org/10.1039/C7TC04661H

[27] Checkol, F., Elfwing, A., Greczynski, G., Mehretie, S., Inganäs, O. and Admassie, S, (2018) Highly Stable and Efficient Lignin-PEDOT/PSS Composites for Removal of Toxic Metals. *Advanced Sustainable Systems*, **2**, Article ID: 1700114. https://doi.org/10.1002/adsu.201700114

[28] Harris, A.R. and Wallace, G.G. (2017) Organic Electrodes and Communications with Excitable Cells. *Advanced Functional Materials*, **28**, Article ID: 1700587. https://doi.org/10.1002/adfm.201700587

[29] Mawad, D., Stewart, E., Officer, D.L., Romeo, T., Wagner, P., Wagner, K. and Wallace, G.G. (2012) A Single Component Conducting Polymer Hydrogel as a Scaffold for Tissue Engineering. *Advanced Functional Materials*, **22**, 2692-2699. https://doi.org/10.1002/adfm.201102373

[30] Kaur, G., Adhikari, R., Cass, P., Bown, M. and Gunatillake, P. (2015) Electrically Conductive Polymers and Composites for Biomedical Applications. *RSC Advances*, **5**, 37553-37567. https://doi.org/10.1039/C5RA01851J

[31] Schmidt, C.E., Shastri, V.R., Vacanti, J.P. and Langer, R. (1997) Stimulation of Neurite Outgrowth Using an Electrically Conducting Polymer. *Proceedings of the National Academy of Sciences of the United States of America*, **94**, 8948-8953. https://doi.org/10.1073/pnas.94.17.8948

[32] Ateh, D.D., Navsaria, H.A. and Vadgama, P. (2006) Polypyrrole-Based Conducting Polymers and Interactions with Biological Tissues. *Journal of the Royal Society Interface*, **3**, 741-752. https://doi.org/10.1098/rsif.2006.0141

[33] Bendrea, A.-D., Cianga, L. and Cianga, I. (2011) Review Paper: Progress in the Field of Conducting Polymers for Tissue Engineering Applications. *Journal of Biomaterials Applications*, **26**, 3-84. https://doi.org/10.1177/0885328211402704

[34] Ateh, D., Navsaria, H. and Vadgama, P. (2006) Polypyrrole-Based Conducting Polymers and Interactions with Biological Tissues. *Journal of The Royal Society Interface*, **3**, 741-752. https://doi.org/10.1098/rsif.2006.0141

[35] Wang, X., Gu, X., Yuan, C., Chen, S., Zhang, P., Zhang, T., Yao, J., Chen, F. and Chen, G. (2004) Evaluation of Biocompatibility of Polypyrrole *in Vitro* and *in Vivo*. *Journal of Biomaterials Applications*, **68A**, 411-422. https://doi.org/10.1002/jbm.a.20065

[36] Wang, L., Wu, Y.B., Hu, T.L., Guo, B.L. and Ma, P.X. (2017) Electrospun Conductive Nanofibrous Scaffolds for Engineering Cardiac Tissue and 3D Bioactuators. *Acta Biomaterialia*, **59**, 68-81. https://doi.org/10.1016/j.actbio.2017.06.036

[37] Wang, L., Wu, Y.B., Guo, B.L. and Ma, P.X. (2015) Nanofiber Yarn/Hydrogel Core-Shell Scaffolds Mimicking Native

Skeletal Muscle Tissue for Guiding 3D Myoblast Alignment, Elongation, and Differentiation. *ACS Nano*, **9**, 9167-9179. https://doi.org/10.1021/acsnano.5b03644

[38] Lukášek, J., Hauzerová, Š., Havlíčková, K., Strnadová, K., Mašek, K., Stuchlík, M., Stibor, I., Jenčová, V. and Řezanka, M. (2019) Cyclodextrin-Polypyrrole Coatings of Scaffolds for Tissue Engineering. *Polymers*, **11**, Article No. 459. https://doi.org/10.3390/polym11030459

[39] Iyoda, M. and Shimizu, H. (2015) Multifunctional π-Expanded Oligothiophene Macrocycles. *Chemical Society Reviews*, **44**, 6411-6424. https://doi.org/10.1039/C5CS00388A

[40] Hussain, S.T., Abbas, F., Kausar, A. and Khan, M.R. (2013) New Polyaniline/Polypyrrole/Polythiophene and Functionalized Multiwalled Carbon Nanotube-Based Nanocomposites: Layer-by-Layer *In Situ* Polymerization. *High Performance Polymers*, **25**, 70-78. https://doi.org/10.1177/0954008312456048

[41] Zhou, L., Yu, M., Chen, X., Nie, S., Lai, W.Y., Su, W., Cui, Z. and Huang, W. (2018) Ito-Free Flexible Electronics:Screen-Printed Poly (3, 4-Ethylenedioxythiophene): Poly (Styrenesulfonate) Grids as ITO-Free Anodes for Flexible Organic Light-Emitting Diodes. *Advanced Functional Materials*, **28**, Article ID: 1870072. https://doi.org/10.1002/adfm.201870072

[42] Du, Z.J., Luo, X., Weaver, C. and Cui, X.T. (2015) Poly(3,4-Ethylenedioxythiophene)-Ionic Liquid Coating Improves Neural Recording and Stimulation Functionality of MEAs. *Journal of Materials Chemistry C*, **3**, 6515-6524. https://doi.org/10.1039/C5TC00145E

[43] Yang, B., Yao, F., Ye, L., Hao, T., Zhang, Y., Zhang, L., Dong, D., Fang, W., Wang, Y., Zhang, X., Wang, C. and Li, J. (2020) A Conductive PEDOT/Alginate Porous Scaffold as a Platform to Modulate the Biological Behaviors of Brown Adipose-Derived Stem Cells. *Biomaterials Science*, **8**, 3173-3185. https://doi.org/10.1039/C9BM02012H

[44] Hatchett, D.W., Josowicz, M. and Ianata, J. (1999) Comparision of Chemically and Electrochemically Synthesized Polyaniline Films. *Journal of the Electrochemical Society*, **146**, 4535-4538. https://doi.org/10.1149/1.1392670

[45] MacDiarmid, A.G., Huang, W., Humphrey, B.D. and Somasiri, N.L.D. (1985) Polyaniline: Protonic Acid Doping to the Metallic Regime. *Molecular Crystals and Liquid Crystals*, **125**, 309-318. https://doi.org/10.1080/00268948508080110

[46] Li, L., Ge, J., Guo, B. and Ma, P.X. (2014) *In Situ* Forming Biodegradable Electroactive Hydrogels. *Polymer Chemistry*, **5**, 2880-2890. https://doi.org/10.1039/C3PY01634J

[47] Rahman, N.A., Feisst, V., Dickinson, M.E., Malmström, J., Dunbar, P.R. and Travas-Sejdic, J. (2013) Functional Polyaniline Nanofibre Mats for Human Adipose-Derived Stem Cell Proliferation and Adhesion. *Materials Chemistry and Physics*, **138**, 333-341. https://doi.org/10.1016/j.matchemphys.2012.11.065

[48] Zarrintaj, P., Vahabi, H., Saeb, M.R. and Mozafari, M. (2019) Chapter 14: Application of Polyaniline and Its Derivatives. In: Mozafari, M. and Chauhan, N.P.S., Eds., *Fundamentals and Emerging Applications of Polyaniline*, Elsevier, Amsterdam, 259-272. https://doi.org/10.1016/B978-0-12-817915-4.00014-2

[49] Zhao, X., Li, P., Guo, B. and Ma, P.X. (2015) Antibacterial and Conductive Injectable Hydrogels Based on Quaternized Chitosan-Graft-Polyaniline/Oxidized Dextran for Tissue Engineering. *Acta Biomaterialia*, **26**, 236-248. https://doi.org/10.1016/j.actbio.2015.08.006

[50] Zhang, X., Qi, H., Wang, S., Feng, L., Ji, Y., Tao, L., Li, S. and Wei, Y. (2012) Cellular Responses of Aniline Oligomers: A Preliminary Study. *Toxicology Research*, **1**, 201-205. https://doi.org/10.1039/c2tx20035j

[51] Qi, H., Liu, M., Xu, L., Feng, L., Tao, L., Ji, Y., Zhang, X. and Wei, Y. (2013) Biocompatibility Evaluation of Aniline Oligomers with Different End-Functional Groups. *Toxicology Research*, **2**, 427-433. https://doi.org/10.1039/c3tx50060h

[52] Ding, H., Zhong, M., Kim, Y.J., Pholpabu, P., Balasubramanian, A., Hui, C.M., He, H., Yang, H., Matyjaszewski, K. and Bettinger, C.J. (2014) Biologically Derived Soft Conducting Hydrogels Using Heparin-Doped Polymer Networks. *ACS Nano*, **8**, 4348-4357. https://doi.org/10.1021/nn406019m

[53] Humpolíček, P., Radaszkiewicz, K.A., Capáková, Z., Pacherník, J., Bober, P., Kašpárková, V., Rejmontová, P., Lehocký, M., Ponížil, P. and Stejskal, J. (2018) Polyaniline Cryogels: Biocompatibility of Novel Conducting Macroporous Material. *Scientific Reports*, **8**, Article No. 135. https://doi.org/10.1038/s41598-017-18290-1

[54] Voskerician, G., Shive, M.S., Shawgo, R.S., von Recum, H., Anderson, J.M., Cima, M.J., *et al*. (2003) Biocompatibility and Biofouling of MEMS Drug Delivery Devices. *Biomaterials*, **24**, 1959-1967. https://doi.org/10.1016/S0142-9612(02)00565-3

[55] Flamme, K., Popat, K.C., Leoni, L., Markiewicz, E., La Tempa, T.J., Roman, B.B., *et al*. (2007) Biocompatibility of Nanoporous Alumina Membranes for Immunoisolation. *Biomaterials*, **28**, 2638-2645. https://doi.org/10.1016/j.biomaterials.2007.02.010

[56] Zhang, M. and Ferrari, M. (1997) Reduction of Albumin Adsorption onto Silicon Surfaces by Tween 20. *Biotechnolo-*

gy & Bioengineering, **56**, 618-625.
https://doi.org/10.1002/(SICI)1097-0290(19971220)56:6%3C618::AID-BIT4%3E3.0.CO;2-Q

[57] Ainslie, K.M. and Desai, T.A. (2012) Microtechnologies for Drug Delivery. In: Wright, J. and Burgess, D., Eds., *Long Acting Injections and Implants*, Springer, Boston, 359-381. https://doi.org/10.1007/978-1-4614-0554-2_18

[58] Tölli, M.A., Ferreira, M.P., Kinnunen, S.M., Rysä, J., Mäkilä, E.M., Szabó, Z., Serpi, R.E., Ohukainen, P.J., Välimäki, M.J. and Correia, A.M. (2014) *In Vivo* Biocompatibility of Porous Silicon Biomaterials for Drug Delivery to the Heart. *Biomaterials*, **35**, 8394-8405. https://doi.org/10.1016/j.biomaterials.2014.05.078

[59] Tan, Y., Richards, D., Xu, R., Stewart-Clark, S., Mani, S.K., Borg, T.K., Menick, D.R., Tian, B. and Mei, Y. (2015) Silicon Nanowire-Induced Maturation of Cardiomyocytes Derived from Human Induced Pluripotent Stem Cells. *Nano Letters*, **15**, 2765-2772. https://doi.org/10.1021/nl502227a

[60] Jogi, B.F., Sawant, M., Kulkarni, M. and Brahmankar, P. (2012) Dispersion and Performance Properties of Carbon Nanotubes (CNTs) Based Polymer Composites: A Review. *Journal of Encapsulation & Adsorption Sciences*, **2**, 69-78. https://doi.org/10.4236/jeas.2012.24010

[61] Kobylko, M., Kociak, M., Sato, Y., Urita, K., Bonnot, A.M., Kasumov, A., *et al*. (2014) Ballistic- and Quantum-Conductor Carbon Nanotubes: A Reference Experiment Put to the Test. *Physical Review B*, **90**, Article ID: 195431. https://doi.org/10.1103/PhysRevB.90.195431

[62] Liu, Z. and Liang, X.J. (2012) Nano-Carbons as Theranostics. *Theranostics*, **2**, 235-237.
https://doi.org/10.7150/thno.4156

[63] Liu, L., Yang, C., Zhao, K., Li, J. and Wu, H.-C. (2013) Ultrashort Single-Walled Carbon Nanotubes in a Lipid Bilayer as a New Nanopore Sensor. *Nature Communications*, **4**, Article No. 2989. https://doi.org/10.1038/ncomms3989

[64] Liu, S. and Guo, X. (2012) Carbon Nanomaterials Field-Effect-Transistor-Based Biosensors. *NPG Asia Materials*, **4**, Article No. e23. https://doi.org/10.1038/am.2012.42

[65] Wang, H. and Dai, H. (2013) ChemInform Abstract: Strongly Coupled Inorganic—Nano-Carbon Hybrid Materials for Energy Storage. *ChemInform*, **44**, n.p. https://doi.org/10.1002/chin.201324189

[66] Kang, Y. (2017) Catalytic Nanomaterials for Energy Conversion and Storage. *China Energy Materials Chemistry Symposium*, Taiyuan, 9 June 2017, 1-2.

[67] Novoselov, K.S., Geim, A.K., Morozov, S.V., Jiang, D., Zhang, Y., Dubonos, S.V., Grigorieva, I.V. and Firsov, A.A. (2004) Electric Field Effect in Atomically Thin Carbon Films. *Science*, **306**, 666-669.
https://doi.org/10.1126/science.1102896

[68] Li, Y., Samad, Y.A., Polychronopoulou, K., Alhassan, S.M. and Liao, K. (2014) Highly Electrically Conductive Nanocomposites Based on Polymer Infused Graphene Sponges. *Scientific Reports*, **4**, Article No. 4652.
https://doi.org/10.1038/srep04652

[69] Menaa, F., Abdelghani, A. and Menaa, B. (2015) Graphene Nanomaterials as Biocompatible and Conductive Scaffolds for Stem Cells: Impact for Tissue Engineering and Regenerative Medicine. *Journal of Tissue Engineering and Regenerative Medicine*, **9**, 1321-1338. https://doi.org/10.1002/term.1910

[70] Song, H.S., Kwon, O.S., Kim, J.-H., Conde, J. and Artzi, N. (2017) 3D hydrogel Scaffold Doped with 2D Graphene Materials for Biosensors and Bioelectronics. *Biosensors and Bioelectronics*, **89**, 187-200.
https://doi.org/10.1016/j.bios.2016.03.045

[71] Talebian, S., Mehrali, M., Raad, R., Safaei, F., Xi, J., Liu, Z. and Foroughi, J. (2020) Electrically Conducting Hydrogel Graphene Nanocomposite Biofibers for Biomedical Applications. *Frontiers in Chemistry*, **8**, Article No. 88.
https://doi.org/10.3389/fchem.2020.00088

[72] Iijima, S. (1991) Helical Microtubles of Graphitic Carbon. *Nature*, **354**, 56-58. https://doi.org/10.1038/354056a0

[73] Huang, J., Liu, Y. and You, T. (2010) Carbon Nanofiber Based Electrochemical Biosensors: A Review. *Analytical Methods*, **2**, 202-211. https://doi.org/10.1039/b9ay00312f

[74] Perhun, T.I., Bychko, I.B. and Trypolsky, A.I. (2013) Catalytic Properties of Graphene Material in the Hydrogenation of Ethylene. *Theoretical and Experimental Chemistry*, **48**, 367-370. https://doi.org/10.1007/s11237-013-9282-1

[75] Bhattacharyya, S., Guillot, S., Dabboue, H., Tranchant, J.-F. and Salvetat, J.-P. (2008) Carbon Nanotubes as Structural Nanofibers for Hyaluronic Acid Hydrogel Scaffolds. *Biomacromolecules*, **9**, 505-509.
https://doi.org/10.1021/bm7009976

[76] Jia, G., Wang, H., Yan, L., Wang, X., Pei, R. and Yan, T. (2005) Cytotoxicity of Carbon Nanomaterials: Single-Wall Nanotube, Multi-Wall Nanotube and Fullerene. *Environmental Science & Technology*, **39**, 1378-1383.
https://doi.org/10.1021/es048729l

[77] Shvedova, A.A., Castranova, V., Kisin, E.R., Schwegler-Berry, D., Murray, A.R., Gandelsman, V.Z., *et al*. (2003) Exposure to Carbon Nanotube Material: Assessment of Nanotube Cytotoxicity Using Human Keratinocyte Cells. *Journal*

of Toxicology and Environmental Health, *Part A*, **66**, 1909-1926. https://doi.org/10.1080/713853956

[78] Cui, D.X., Tian, F.R., Ozkan, C.S., Wang, M. and Gao, H.J. (2005) Effect of Single Wall Carbon Nanotubes on Human HEK293 Cells. *Toxicology Letters*, **55**, 73-85. https://doi.org/10.1016/j.toxlet.2004.08.015

[79] Sperling, R.A., Rivera, Gil, P., Zhang, F., Zanella, M. and Parak, W.J. (2008) Biological Applications of Gold Nanoparticles. *Chemical Society Reviews*, **37**, 1896-908. https://doi.org/10.1039/b712170a

[80] McKeon-Fischer, K.D. and Freeman, J.W. (2011) Characterization of Electrospun Poly(L-Lactide) and Gold Nanoparticle Composite Scaffolds for Skeletal Muscle Tissue Engineering. *Journal of Tissue Engineering and Regenerative Medicine*, **5**, 560-568. https://doi.org/10.1002/term.348