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前列腺癌放射组学与多组学综合研究：现状、挑战与未来方向

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摘　要

前列腺癌的精确诊断及预后评估对于优化治疗策略和改善患者结局至关重要。放射组学和多组学技术的兴起为前列腺癌的研究带来了新的视角。放射组学通过高通量提取影像图像定量特征，实现肿瘤内部异质性可视化并揭示影像图像的潜在预后生物学信息；而多组学技术通过整合基因组学、转录组学、蛋白组学和代谢组学等多维数据，为癌症的全面分析和精准治疗提供了可能性。本文综述聚焦于放射组学与多组学在前列腺癌中的研究现状，探讨了相关研究中的争议与挑战，并展望未来发展趋势。

关键词

前列腺癌，放射组学，多组学，多模态

Integrated Research of Prostate Cancer Radiomics and Multi-Omics: Current Status, Challenges and Future Directions

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Abstract

Accurate diagnosis and prognostic assessment of prostate cancer are of paramount importance in optimizing treatment regimens and ameliorating patient outcomes. The advent of radiomics and multi-omics technologies has bestowed novel vistas upon prostate cancer research. Radiomics

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facilitates the visualization of intratumoral heterogeneity and unearths the latent prognostic biological information within imaging images via high-throughput extraction of quantitative features therefrom. Multi-omics technologies, by integrating multi-dimensional data including genomics, transcriptomics, proteomics, and metabolomics, furnish the feasibility for comprehensive cancer analysis and precision therapeutics. This review centers on the extant research panorama of radiomics and multi-omics within the domain of prostate cancer, delves into the disputes and hurdles extant in pertinent research, and prognosticates the forthcoming developmental trajectories.

Keywords

Prostate Cancer, Radiomics, Multi-Omics, Multimodal

1. 引言

前列腺癌在全球男性健康领域中占据着重要地位，已成为男性最常见的恶性肿瘤之一，其发病率随年龄增长而逐年上升[1] [2]。由于前列腺癌具有显著且复杂的生物学特性及高度异质性[3]，不同患者之间肿瘤的生物学行为存在显著差异，且这种差异与预后紧密相关[4]。因此，前列腺癌的个体化治疗面临巨大挑战，精准的早期诊断及准确的预后评估对于制定个性化治疗方案至关重要。

目前，传统的前列腺癌诊断主要依赖血清前列腺特异抗原(PSA)检测、直肠指检(DRE)和多参数磁共振成像(mpMRI) [5]-[7]。然而，这些方法存在一定局限性，如 PSA 检测的特异性较低，容易导致过度诊断和治疗[8]。此外，尽管手术、放疗和激素治疗是常见的治疗方式，但它们往往难以根据个体患者的具体病情进行精准调整[9]。

近年来，放射组学和多组学技术的兴起为前列腺癌的研究提供了新的视角。放射组学是一种从医学影像中高通量提取定量特征，进而分析和预测肿瘤生物学行为的技术。与传统影像学分析方法相比，放射组学能够揭示影像数据中的更丰富信息，通过无创手段获取肿瘤血流灌注、细胞外水含量等定量数据，进而实现肿瘤内部异质性可视化[10]-[13]。多组学技术则通过整合不同层次的生物学数据，提供了全面的癌症研究框架，为个性化治疗提供了新的可能[14] [15]。本文将综述放射组学及多组学综合研究在前列腺癌中的应用进展。

2. 放射组学与前列腺癌

2.1. 放射组学概述

放射组学作为一种依据影像数据展开定量分析的技术，在 2012 年由荷兰学者 Lambin 首度提出[16]。其借助对医学影像图像的深度剖析，以高通量方式提取诸如形态学特征(如大小、形状、边缘等)、灰度直方图特征、纹理特征等定量特征[17]。而这些提取出的特征能够精准映射组织的微观结构与功能状态，进而在肿瘤的诊断、分期以及治疗方面贡献关键信息[18]。放射组学的工作流程通常包括以下几个步骤：(1) 图像获取(常采用如 mpMRI 与 CT 等标准化成像技术作为起始环节)、(2) 图像分割(将感兴趣区域即 ROI 从背景分离)、(3) 特征提取(从分割后的 ROI 提取大量定量特征)、(4) 特征选择(借助主成分分析及随机森林算法等减少特征维度并消除冗余)以及(5) 模型构建(运用机器学习或统计方法构建分类或预测模型)

[19] [20]。

2.2. 放射组学在前列腺癌中的应用

前列腺癌的放射组学研究多以多参数磁共振成像(mpMRI)数据为基础，涵盖 T1 加权像、T2 加权像、弥散加权成像(DWI)及动态对比增强成像(DCE)等序列。前列腺癌在生物学特性上呈现显著的异质性，导致肿瘤预后具有较大的可变性。尽管大多数前列腺癌为惰性病变，但少数则具备高侵袭性，甚至威胁生命。放射组学技术通过非侵入性手段，能够精准捕捉前列腺癌影像学层面的异质性特征，主要通过像素密度量化和空间分布模式分析来实现。大量研究表明，这种影像学特征与前列腺癌的侵袭性生物学行为、病理分级体系、疾病预后及治疗反应等临床要素密切相关[16]。例如，Cuocolo 等[21]通过分析 mpMRI 图像形态学特征，成功区分临床显著性与无临床意义的前列腺癌，减少不必要的活检。在病理分期评估方面，一些影像特征与 Gleason 评分密切相关，有助于精确分期和个性化治疗方案的制定[22]。对于预后，基于放射组学特征构建的预测模型可有效评估患者的生存期与复发风险。例如，Rizzo 等[23]发现影像纹理的异质性与肿瘤边缘复杂度及不良预后之间有着紧密的关联；Jia 等[24]基于放射组学与临床数据构建的混合模型则能够有效预测前列腺癌患者的无进展生存期(PFS)，并为临床提供非侵入性的风险分层工具。在治疗方面，放射组学通过分析治疗前后影像变化，能够预测患者对放疗和药物治疗的反应，进而评估对特定治疗的敏感性，从而优化治疗策略[25]。

3. 多组学研究与前列腺癌

3.1. 多组学研究概述

多组学研究作为一种综合性与系统性的生物学研究策略，可同步对生物系统内多种层次的生物分子信息予以分析，以此深入且全面地把握生物系统的复杂性、功能特性及动态演变历程[26]。其核心目标在于整合基因组学、转录组学、蛋白组学以及代谢组学等不同类型的生物学数据，进而全方位解析前列腺癌的发生发展机制[27]。多组学数据的整合往往需借助先进的生物信息学及计算生物学工具，诸如相关性网络分析、机器学习或深度学习算法与贝叶斯网络等。凭借这些方法，能够有效揭示不同组学层次间的内在关联与相互作用，为生物学研究提供更为完备的认知视角[28]。

3.2. 多组学数据分析方法

3.2.1. 相关性网络分析及数据网络

在多组学数据集成中，常采用分析不同组学数据之间相关性或共映射的方法。这些分析揭示了基因组、转录组、蛋白质组和代谢组等数据间的一致性或差异性趋势，帮助识别生物过程中的关键联系[29] [30]。通过网络分析方法，研究者将多组学分子视为网络节点，探讨基因、蛋白质和代谢物之间的相互作用，以及潜在的生物途径子网络[31]。然而，由于多组学数据的复杂性，综合分析需要复杂的算法支持[32]，同时验证结果也具有一定困难。因此，开源工具和共享数据库(如 netOmics、MetaboAnalyst 5.0、MergeOmics 2.0) [33]-[35]在数据整合和分析中发挥了重要作用，为深入推动生物医学研究提供了技术支撑。

3.2.2. 深度学习或机器学习算法

随着高通量组学技术的发展，深度学习和机器学习在多组学数据整合中的应用为精准医学提供了重要支持，尤其是在生物标志物发现方面[27] [36]。主要的多数据整合方法包括：

1) 串联整合：将不同组学数据与表型信息结合，形成多组学数据矩阵，通过监督或非监督学习进行分析。例如，将基因表达、拷贝数变异和突变数据整合后，利用随机森林和支持向量机等算法预测抗癌药物反应[37] [38]。

2) 模型整合：利用不同组学数据生成独立模型，然后将多个模型整合为综合模型。例如，Ogbonnaya等[39]构建的放射组学与基因组学联合预测模型在前列腺癌分级预测方面取得了显著提升；Avasthi 等[40]利用 miRNA 与 MR-T2W、MR-ADC 特征组合构建的多变量模型在识别前列腺癌侵袭性方面表现出色。

3) 转换整合：通过将组学数据转换为中间形式(如图形或核矩阵)，在制定模型前进行整合，提升分类性能。比如，利用图卷积网络整合相似性网络描述的组学特征[41]。

这些方法提高了数据整合的效率与准确性，为精准医学的实施提供了坚实的技术基础。

3.3. 多组学数据的整合分析进展

3.3.1. 单细胞多组学

单细胞组学技术(如 scRNA-seq、scDNA-seq 和单细胞蛋白质组学)为深入研究前列腺癌的异质性和肿瘤微环境提供了重要工具[42]。研究发现，前列腺癌细胞和肿瘤微环境中的 lncRNAs 变化与疾病进展密切相关，具有潜在的预后标志物价值[43]。此外，基因组测序和转录组分析揭示了前列腺癌遗传异质性及其与临床特征的关联。Ren 等[44]对 65 例未经治疗的前列腺癌患者进行基因组和转录组分析，发现中国患者中 CHD1 缺失频率较高，且与 AR 上游激活基因突变多和 TMPRSS2-ERG 融合率低相关。他们还确认 PCDH9 为关键肿瘤抑制基因，而 PLXNA1 的扩增与转移及较差存活率相关。这些发现揭示了前列腺癌的遗传异质性，并为新治疗靶点和预后标志物的识别提供了依据。Kirk 等[45]通过多组学方法创建小鼠单细胞参考图谱，发现去势抵抗性管腔细胞与尿道近端干细胞/祖细胞不同，且 AP1、WNT/β-catenin、FOXQ1、NF-κB 和 JAK/STAT 通路是其主要驱动因素。单细胞组学技术还促进了对去势抵抗性前列腺癌的深入理解[46]，并加深了我们对前列腺癌异质性的理解，为治疗靶点和精准治疗策略提供了强有力的工具。

3.3.2. 空间多组学

空间多组学技术通过整合不同空间尺度的数据，提供了对前列腺癌异质性的全新理解[47]。Quan 等[48]研究表明，空间转录组测序揭示了前列腺癌的多灶性和肿瘤内异质性，确定了与 Gleason 评分相关的关键基因，这为疾病分子分型和预后评估提供了新的生物标志物。此外，De Vargas Roditi 等[49]利用空间多组学技术发现了与高分级前列腺癌相关的细胞亚群，揭示了肿瘤微环境的复杂性，为免疫治疗和靶向治疗提供了新的研究方向。Bian 等[50]通过 scRNA-seq、空间转录组学和 ATAC-seq，鉴定出以高 SOX9 和低 AR 表达为特征的俱乐部细胞亚群，表明这些细胞在前列腺癌进展中具有重要作用。这些干细胞亚群的发现为耐药性和复发性前列腺癌的治疗提供了新的靶点。

总之，多组学数据的整合深化了我们对前列腺癌的理解，并为精准诊断和治疗策略的开发提供了强有力的支持。

4. 单组学研究在前列腺癌中应用进展

4.1. 基因组学

基因组学聚焦于基因突变、拷贝数变异、表观遗传修饰及 DNA 甲基化等方面[51]。在前列腺癌研究中，Taşan 等[52]通过全基因组关联研究发现多个易感位点，但这些位点在不同人群和环境中的作用机制可能不同。Chopra 等[53]揭示，在家族性前列腺癌遗传背景下，个体罹患前列腺癌的概率可达 50%，强调遗传因素在早期筛查中的重要性。前列腺癌的基因突变谱复杂，其中 TP53、PTEN 和 RB1 基因突变与不良预后相关[54] [55]，但其对治疗响应的影响仍需进一步研究，具体而言，需探讨 TP53 突变是否增加对某些治疗的抵抗性，以及 PTEN 和 RB1 的变异是否预测对特定治疗的敏感性。这些研究为新治疗策略和预后评估提供了重要依据。

4.2. 转录组学

转录组学技术能够精准评估基因调控网络和 mRNA 表达动态，尤其在肿瘤亚型识别中具有重要意义[56] [57]。在前列腺癌研究中，Eke 等[58]发现，放疗后非编码 RNA (ncRNA)表达上升，可能与不良预后相关，提示 ncRNAs 监测可能成为预测预后的重要生物指标，但其临床应用仍需进一步验证。Zhao 等[59]识别出与前列腺癌进展和不良预后相关的高谱系可塑性细胞群(LPC)，并确定 HMMR 为标志物，为理解前列腺癌的异质性和进展机制提供了新视角。这些细胞群和标志物的临床应用、特异性和敏感性需要更深入探讨。Chen 等[60]发现 KLK3 的异位表达与微转移相关，提示 KLK3 可能是潜在的治疗靶点。转录组学研究揭示了前列腺癌的生物学特性，特别是在放疗反应、肿瘤异质性、标志物识别和微转移机制方面。为了将这些发现转化为临床应用，需要进行深入的机制研究，并在不同患者群体中验证其有效性。

4.3. 蛋白质组学

蛋白质组学研究反映细胞活动和生物成分失调[61] [62]，在前列腺癌的诊断和管理中具有重要作用。Tonry 等[63]强调，蛋白质组学在生物标志物驱动的决策工具中潜力巨大。Katsogiannou 等[64]通过质谱技术鉴定出 28 种与前列腺癌相关的蛋白质，涉及 MAPK、ERK、TGFB1 和泛素化途径，这些蛋白质可能在前列腺癌发展中起关键作用。Davalieva 等[65]通过二维凝胶电泳(2D-DGE)和 Western blotting 技术，鉴定出 UBE2N、丝氨酸/三蛋白磷酸酶 PP1β (PPP1CB)和 PSMB6 等多种蛋白作为前列腺癌的生物标志物。SMARCA4 的缺失可能影响 CRPC 的发育和传播[66]，为治疗新靶点的开发提供了线索，这可能对改善 CRPC 患者的预后具有重要意义。蛋白质组学在早期诊断、预后评估及治疗反应监测中有重要应用。

4.4. 代谢组学

代谢组学通过对代谢产物的量化和表征，揭示疾病成因并为新型生物标志物的发现提供线索[67]。在前列腺癌中，代谢组学帮助识别特定代谢谱，成为潜在的临床生物标志物[68]。Kumar 等[69]通过 ^{1}H-NMR 分析血清样本，发现代谢谱可用于前列腺癌的早期诊断。Giunchi 和 Gómez-Cebrián 等[70] [71]研究发现，前列腺癌组织在脂质、核苷酸和 TCA 循环等方面存在显著差异，揭示了前列腺癌特有的代谢变化，为开发新的治疗策略提供了方向。此外，尿液代谢组学也被证明在前列腺癌的诊断和预后评估中具有重要价值[72] [73]。无论是代谢特征分析，还是不同样本类型的代谢组学应用，都为前列腺癌的诊断及病情判断等提供了有力依据，未来有望进一步助力前列腺癌的精准诊疗。

5. 放射组学与多组学整合研究在前列腺癌中应用进展

5.1. 放射组学与基因组学整合

放射组学与基因组学的整合研究揭示了影像特征与基因之间的内在关联性。McCann 等[74]的研究发现，前列腺多参数 MRI 的定量动态对比增强 MRI 特征 k(ep)与前列腺癌外周区 PTEN 基因表达之间存在显著相关性($r = -0.35$, $p = 0.02$)。Ogbonnaya 等[39]提出的创新性放射组学与基因组学联合预测模型在前列腺癌分级预测中表现出卓越的效能，曲线下面积(AUC)高达 0.95。该研究还证实了放射纹理特征与局部前列腺癌微环境中的细胞凋亡、缺氧状态以及雄激素受体基因型之间的深刻生物学关联。通过将影像数据与基因信息结合，不仅能挖掘潜在的生物标志物，还为深入探讨前列腺癌的病理生理过程提供了多维度视角。

5.2. 放射组学与转录组学整合

放射组学与转录组学的整合为揭示影像特征与转录异质性提供了新的探索方向。Dinis Fernandes 等

[75]通过提取多参数 MRI 序列(T2W, DWI, DCE)的纹理影像特征，结合磁共振色散成像(MRDI)药代动力学图与同步转录组学分析，发现 31 个影像特征与 33 个转录组学特征显著相关，如 MRDI A 中位数与转录因子 STAT6 和 TFAP2A 的活性相关。Avasthi 等[40]的研究表明，在识别临床侵袭性前列腺癌时，miRNA 与 MR-T2W、MR-ADC 特征组合构建的多变量模型效能显著优于单变量模型，AUC 分别为 0.88、0.95 (多变量)与 0.76、0.82、0.84 (单变量)。这些研究为理解前列腺癌的基因代谢重编程提供了新的视角。

5.3. 放射组学与代谢组学整合

放射组学与代谢组学的整合揭示了影像特征与肿瘤代谢产物之间的关系，提供了理解前列腺癌代谢编程的新视角。Zhang 等[76]通过联合分析前列腺癌患者在碳离子放疗(CIRT)前后的 MRI 放射组学特征与尿液代谢组学，发现 CIRT 后患者尿液中 49 种代谢物显著下调，主要富集在半胱氨酸、蛋氨酸等代谢通路中。在 104 个放射组学特征中，33 个与蛋氨酸变化程度显著相关。特别是对比度、差异方差、小依赖高灰度强调和平均绝对偏差这 4 个特征与 BCR 状态密切相关，其 AUC 为 0.704~0.769。将放射组学与代谢组学结合，有助于挖掘生物标志物与代谢通路的联系，深化对前列腺癌发病机制的理解。

6. 多组学整合研究的争议与挑战

6.1. 数据的异质性与标准化

不同研究中心的成像设备与操作标准差异导致放射组学数据存在显著异质性，影响数据的可比性和模型的泛化能力[77]。在多组学整合研究中，数据标准化同样面临挑战。尽管当前已有多组学研究和数据库，但特定生物实体的多组学数据检索仍存在障碍，数据分散于不同平台且缺乏有效的跨平台整合机制，遵循 FAIR 原则面临困难[78] [79]。大型项目有专属的数据共享途径，但小型研究在依赖公共数据库时，常忽视数据集的多组学特性，缺乏统一的框架和标准[80]。

6.2. 整合模型的可解释性

多组学整合模型在预测准确性上表现优异，但其复杂性和“黑箱”特性限制了其在临床应用中的可解释性[81]。目前，大多数模型的可解释性仅限于识别生物标志物及其相关生物过程的初步分析。功能富集分析作为常用的多组学数据解释工具，可单独应用于每种组学，或联合应用于多组学数据的综合分析[82] [83]。尽管这类方法能在一定程度上揭示受影响的生物过程，但在深入挖掘跨分子层次机制时仍存在局限[77]。目前的多组学模型多为静态展示结果，缺乏动态数学模型和交互式可视化方案。未来的研究应聚焦于提升模型可解释性，开发融合多层次规则的计算方法[23]。

6.3. 模型性能与可扩展性

多组学数据集具有规模庞大且结构复杂的特点，随着研究的深入，面临更大的挑战，尤其是在整合患者队列数据、成像数据和单细胞组学数据时[77] [84] [85]。处理大规模多组学数据的过程中，对计算能力提出了更高要求。由于跨组学数据的高度多样性，设计通用的“一刀切”解决方案几乎不可能。因此，需要为每种特定类型的组学数据定制专门的计算解决方案[86]。

7. 小结和展望

前列腺癌放射组学及多组学综合研究在精确诊断、风险预测及预后评估等方面取得了显著进展，为深入了解前列腺癌的发病机制、寻找潜在的预后标志物和治疗靶点提供了重要的依据。然而，目前的研究仍存在一些局限性，如多组学数据的质量控制、数据整合方法的优化、临床验证的不足等。未来，需要进一步加强多组学研究的规范化和标准化，优化数据整合方法，加强临床验证，以推动前列腺癌多组

学研究在临床实践中的应用，为前列腺癌患者的精准治疗和预后改善提供更好的支持。

参考文献

[1] Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R.L., Soerjomataram, I., *et al*. (2024) Global Cancer Statistics 2022: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA*: *A Cancer Journal for Clinicians*, **74**, 229-263. https://doi.org/10.3322/caac.21834

[2] Siegel, R.L., Giaquinto, A.N. and Jemal, A. (2024) Cancer Statistics, 2024. *CA*: *A Cancer Journal for Clinicians*, **74**, 12-49. https://doi.org/10.3322/caac.21820

[3] Berenguer, C.V., Pereira, F., Câmara, J.S. and Pereira, J.A.M. (2023) Underlying Features of Prostate Cancer—Statistics, Risk Factors, and Emerging Methods for Its Diagnosis. *Current Oncology*, **30**, 2300-2321. https://doi.org/10.3390/curroncol30020178

[4] Haffner, M.C., Zwart, W., Roudier, M.P., True, L.D., Nelson, W.G., Epstein, J.I., *et al*. (2020) Genomic and Phenotypic Heterogeneity in Prostate Cancer. *Nature Reviews Urology*, **18**, 79-92. https://doi.org/10.1038/s41585-020-00400-w

[5] Ilic, D., Djulbegovic, M., Jung, J.H., Hwang, E.C., Zhou, Q., Cleves, A., *et al*. (2018) Prostate Cancer Screening with Prostate-Specific Antigen (PSA) Test: A Systematic Review and Meta-Analysis. *BMJ*, **362**, k3519. https://doi.org/10.1136/bmj.k3519

[6] Shish, L. and Zabell, J. (2024) Digital Rectal Exam in Prostate Cancer Screening and Elevated PSA Work-Up—Is There a Role Anymore? *Current Urology Reports*, **25**, 193-199. https://doi.org/10.1007/s11934-024-01218-4

[7] 姜红坚, 成艳平. 磁共振成像在前列腺癌诊断中的应用价值[J]. 影像研究与医学应用, 2024, 8(22): 152-154.

[8] Mottet, N., van den Bergh, R.C.N., Briers, E., Van den Broeck, T., Cumberbatch, M.G., De Santis, M., *et al*. (2021) EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer—2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. *European Urology*, **79**, 243-262. https://doi.org/10.1016/j.eururo.2020.09.042

[9] Wilt, T.J., Jones, K.M., Barry, M.J., Andriole, G.L., Culkin, D., Wheeler, T., *et al*. (2017) Follow-Up of Prostatectomy versus Observation for Early Prostate Cancer. *New England Journal of Medicine*, **377**, 132-142. https://doi.org/10.1056/nejmoa1615869

[10] Gillies, R.J., Kinahan, P.E. and Hricak, H. (2016) Radiomics: Images Are More than Pictures, They Are Data. *Radiology*, **278**, 563-577. https://doi.org/10.1148/radiol.2015151169

[11] Gu, R., Tan, S., Xu, Y., Pan, D., Wang, C., Zhao, M., *et al*. (2023) CT Radiomics Prediction of CXCL9 Expression and Survival in Ovarian Cancer. *Journal of Ovarian Research*, **16**, Article No. 180. https://doi.org/10.1186/s13048-023-01248-5

[12] Mossinelli, C., Tagliabue, M., Ruju, F., Cammarata, G., Volpe, S., Raimondi, S., *et al*. (2023) The Role of Radiomics in Tongue Cancer: A New Tool for Prognosis Prediction. *Head & Neck*, **45**, 849-861. https://doi.org/10.1002/hed.27299

[13] Chen, Q., Shao, J., Xue, T., Peng, H., Li, M., Duan, S., *et al*. (2022) Intratumoral and Peritumoral Radiomics Nomograms for the Preoperative Prediction of Lymphovascular Invasion and Overall Survival in Non-Small Cell Lung Cancer. *European Radiology*, **33**, 947-958. https://doi.org/10.1007/s00330-022-09109-3

[14] He, X., Liu, X., Zuo, F., Shi, H. and Jing, J. (2023) Artificial Intelligence-Based Multi-Omics Analysis Fuels Cancer Precision Medicine. *Seminars in Cancer Biology*, **88**, 187-200. https://doi.org/10.1016/j.semcancer.2022.12.009

[15] Li, L., Sun, M., Wang, J. and Wan, S. (2024) Multi-Omics Based Artificial Intelligence for Cancer Research. *Advances in Cancer Research*, **163**, 303-356. https://doi.org/10.1016/bs.acr.2024.06.005

[16] Lambin, P., Rios-Velazquez, E., Leijenaar, R., Carvalho, S., van Stiphout, R.G.P.M., Granton, P., *et al*. (2012) Radiomics: Extracting More Information from Medical Images Using Advanced Feature Analysis. *European Journal of Cancer*, **48**, 441-446. https://doi.org/10.1016/j.ejca.2011.11.036

[17] Ferrari, R., Trinci, M., Casinelli, A., Treballi, F., Leone, E., Caruso, D., *et al*. (2024) Radiomics in Radiology: What the Radiologist Needs to Know about Technical Aspects and Clinical Impact. *La Radiologia Medica*, **129**, 1751-1765. https://doi.org/10.1007/s11547-024-01904-w

[18] Wen, Y.L. and Leech, M. (2020) Review of the Role of Radiomics in Tumour Risk Classification and Prognosis of Cancer. *Anticancer Research*, **40**, 3605-3618. https://doi.org/10.21873/anticanres.14350

[19] 马晓辉, 周海春, 梁佳伟, 等. 人工智能时代的放射组学及 Pyradiomics 工具包在放射组学中的应用[J]. 浙江医学, 2022, 44(8): 887-889, 895.

[20] Aerts, H.J.W.L., Velazquez, E.R., Leijenaar, R.T.H., Parmar, C., Grossmann, P., Carvalho, S., *et al*. (2014) Decoding Tumour Phenotype by Noninvasive Imaging Using a Quantitative Radiomics Approach. *Nature Communications*, **5**, Article No. 4006. https://doi.org/10.1038/ncomms5006

[21] Cuocolo, R., Stanzione, A., Ponsiglione, A., Romeo, V., Verde, F., Creta, M., *et al*. (2019) Clinically Significant Prostate Cancer Detection on MRI: A Radiomic Shape Features Study. *European Journal of Radiology*, **116**, 144-149. https://doi.org/10.1016/j.ejrad.2019.05.006

[22] Hectors, S.J., Cherny, M., Yadav, K.K., Beksaç, A.T., Thulasidass, H., Lewis, S., *et al*. (2019) Radiomics Features Measured with Multiparametric Magnetic Resonance Imaging Predict Prostate Cancer Aggressiveness. *Journal of Urology*, **202**, 498-505. https://doi.org/10.1097/ju.0000000000000272

[23] Rizzo, S., Botta, F., Raimondi, S., Origgi, D., Fanciullo, C., Morganti, A.G., *et al*. (2018) Radiomics: The Facts and the Challenges of Image Analysis. *European Radiology Experimental*, **2**, Article No. 36. https://doi.org/10.1186/s41747-018-0068-z

[24] Jia, Y., Quan, S., Ren, J., Wu, H., Liu, A., Gao, Y., *et al*. (2022) MRI Radiomics Predicts Progression-Free Survival in Prostate Cancer. *Frontiers in Oncology*, **12**, Article 974257. https://doi.org/10.3389/fonc.2022.974257

[25] Norris, J.M., Simpson, B.S., Parry, M.A., Allen, C., Ball, R., Freeman, A., *et al*. (2020) Genetic Landscape of Prostate Cancer Conspicuity on Multiparametric Magnetic Resonance Imaging: A Systematic Review and Bioinformatic Analysis. *European Urology Open Science*, **20**, 37-47. https://doi.org/10.1016/j.euros.2020.06.006

[26] Srivastava, R. (2022) Applications of Artificial Intelligence Multiomics in Precision Oncology. *Journal of Cancer Research and Clinical Oncology*, **149**, 503-510. https://doi.org/10.1007/s00432-022-04161-4

[27] Medori, M.C., Micheletti, C., Gadler, M., *et al*. (2023) Omics Sciences and Precision Medicine in Prostate Cancer. *La Clinica Terapeutica*, **174**, 95-103. https://doi.org/10.7417/CT.2023.2476

[28] Chen, C., Wang, J., Pan, D., Wang, X., Xu, Y., Yan, J., *et al*. (2023) Applications of Multi-Omics Analysis in Human Diseases. *MedComm*, **4**, e315. https://doi.org/10.1002/mco2.315

[29] Wang, D., Eraslan, B., Wieland, T., Hallström, B., Hopf, T., Zolg, D.P., *et al*. (2019) A Deep Proteome and Transcriptome Abundance Atlas of 29 Healthy Human Tissues. *Molecular Systems Biology*, **15**, e8503. https://doi.org/10.15252/msb.20188503

[30] Kumar, D., Bansal, G., Narang, A., Basak, T., Abbas, T. and Dash, D. (2016) Integrating Transcriptome and Proteome Profiling: Strategies and Applications. *PROTEOMICS*, **16**, 2533-2544. https://doi.org/10.1002/pmic.201600140

[31] Inge, M.M., Miller, R., Hook, H., Bray, D., Keenan, J.L., Zhao, R., *et al*. (2024) Rapid Profiling of Transcription Factor-Cofactor Interaction Networks Reveals Principles of Epigenetic Regulation. *Nucleic Acids Research*, **52**, 10276-10296. https://doi.org/10.1093/nar/gkae706

[32] Valdeolivas, A., Tichit, L., Navarro, C., Perrin, S., Odelin, G., Levy, N., *et al*. (2018) Random Walk with Restart on Multiplex and Heterogeneous Biological Networks. *Bioinformatics*, **35**, 497-505. https://doi.org/10.1093/bioinformatics/bty637

[33] Bodein, A., Scott-Boyer, M., Perin, O., Lê Cao, K. and Droit, A. (2021) Interpretation of Network-Based Integration from Multi-Omics Longitudinal Data. *Nucleic Acids Research*, **50**, e27-e27. https://doi.org/10.1093/nar/gkab1200

[34] Pang, Z., Zhou, G., Ewald, J., Chang, L., Hacariz, O., Basu, N., *et al*. (2022) Using Metaboanalyst 5.0 for LC-HRMS Spectra Processing, Multi-Omics Integration and Covariate Adjustment of Global Metabolomics Data. *Nature Protocols*, **17**, 1735-1761. https://doi.org/10.1038/s41596-022-00710-w

[35] Ding, J., Blencowe, M., Nghiem, T., Ha, S., Chen, Y., Li, G., *et al*. (2021) Mergeomics 2.0: A Web Server for Multi-Omics Data Integration to Elucidate Disease Networks and Predict Therapeutics. *Nucleic Acids Research*, **49**, W375-W387. https://doi.org/10.1093/nar/gkab405

[36] Delavan, B., Roberts, R., Huang, R., Bao, W., Tong, W. and Liu, Z. (2018) Computational Drug Repositioning for Rare Diseases in the Era of Precision Medicine. *Drug Discovery Today*, **23**, 382-394. https://doi.org/10.1016/j.drudis.2017.10.009

[37] Stetson, L.C., Pearl, T., Chen, Y. and Barnholtz-Sloan, J.S. (2014) Computational Identification of Multi-Omic Correlates of Anticancer Therapeutic Response. *BMC Genomics*, **15**, Article No. S2. https://doi.org/10.1186/1471-2164-15-s7-s2

[38] Fridley, B.L., Lund, S., Jenkins, G.D. and Wang, L. (2012) A Bayesian Integrative Genomic Model for Pathway Analysis of Complex Traits. *Genetic Epidemiology*, **36**, 352-359. https://doi.org/10.1002/gepi.21628

[39] Ogbonnaya, C.N., Alsaedi, B.S.O., Alhussaini, A.J., Hislop, R., Pratt, N., Steele, J.D., *et al*. (2024) Radiogenomics Map-Based Molecular and Imaging Phenotypical Characterization in Localised Prostate Cancer Using Pre-Biopsy Biparametric MR Imaging. *International Journal of Molecular Sciences*, **25**, Article 5379. https://doi.org/10.3390/ijms25105379

[40] Avasthi, K. K., Choi, J., Glushko, T., *et al*. (2024) Extracellular Microvesicle MicroRNAs, along with Imaging Metrics, Improve Detection of Aggressive Prostate Cancer. https://doi.org/10.1101/2024.08.23.24312491

[41] Wang, T., Shao, W., Huang, Z., Tang, H., Zhang, J., Ding, Z., *et al*. (2021) MOGONET Integrates Multi-Omics Data

Using Graph Convolutional Networks Allowing Patient Classification and Biomarker Identification. *Nature Communications*, **12**, Article No. 3445. https://doi.org/10.1038/s41467-021-23774-w

[42] Hachem, S., Yehya, A., El Masri, J., Mavingire, N., Johnson, J.R., Dwead, A.M., *et al*. (2024) Contemporary Update on Clinical and Experimental Prostate Cancer Biomarkers: A Multi-Omics-Focused Approach to Detection and Risk Stratification. *Biology*, **13**, Article 762. https://doi.org/10.3390/biology13100762

[43] Saha, D., Dang, H.X., Zhang, M., Quigley, D.A., Feng, F.Y. and Maher, C.A. (2024) Single Cell-Transcriptomic Analysis Informs the LncRNA Landscape in Metastatic Castration Resistant Prostate Cancer. *npj Genomic Medicine*, **9**, Article No. 14. https://doi.org/10.1038/s41525-024-00401-3

[44] Ren, S., Wei, G., Liu, D., Wang, L., Hou, Y., Zhu, S., *et al*. (2018) Whole-Genome and Transcriptome Sequencing of Prostate Cancer Identify New Genetic Alterations Driving Disease Progression. *European Urology*, **73**, 322-339. https://doi.org/10.1016/j.eururo.2017.08.027

[45] Kirk, J.S., Wang, J., Long, M., Rosario, S., Tracz, A., Ji, Y., *et al*. (2024) Integrated Single-Cell Analysis Defines the Epigenetic Basis of Castration-Resistant Prostate Luminal Cells. *Cell Stem Cell*, **31**, 1203-1221.e7. https://doi.org/10.1016/j.stem.2024.05.008

[46] Wang, Z., Li, Y., Zhao, W., Jiang, S., Huang, Y., Hou, J., *et al*. (2023) Integrative Multi-Omics and Drug-Response Characterization of Patient-Derived Prostate Cancer Primary Cells. *Signal Transduction and Targeted Therapy*, **8**, Article No. 175. https://doi.org/10.1038/s41392-023-01393-9

[47] Hachem, S., Yehya, A., El Masri, J., Mavingire, N., Johnson, J.R., Dwead, A.M., *et al*. (2024) Contemporary Update on Clinical and Experimental Prostate Cancer Biomarkers: A Multi-Omics-Focused Approach to Detection and Risk Stratification. *Biology*, **13**, Article 762. https://doi.org/10.3390/biology13100762

[48] Quan, Y., Zhang, H., Wang, M. and Ping, H. (2023) Visium Spatial Transcriptomics Reveals Intratumor Heterogeneity and Profiles of Gleason Score Progression in Prostate Cancer. *iScience*, **26**, Article 108429. https://doi.org/10.1016/j.isci.2023.108429

[49] De Vargas Roditi, L., Jacobs, A., Rueschoff, J.H., Bankhead, P., Chevrier, S., Jackson, H.W., *et al*. (2022) Single-Cell Proteomics Defines the Cellular Heterogeneity of Localized Prostate Cancer. *Cell Reports Medicine*, **3**, Article 100604. https://doi.org/10.1016/j.xcrm.2022.100604

[50] Bian, X., Wang, W., Abudurexiti, M., Zhang, X., Ma, W., Shi, G., *et al*. (2024) Integration Analysis of Single-Cell Multiomics Reveals Prostate Cancer Heterogeneity. *Advanced Science*, **11**, Article 2305724. https://doi.org/10.1002/advs.202305724

[51] Paolillo, C., Londin, E. and Fortina, P. (2016) Next Generation Sequencing in Cancer: Opportunities and Challenges for Precision Cancer Medicine. *Scandinavian Journal of Clinical and Laboratory Investigation*, **76**, S84-S91. https://doi.org/10.1080/00365513.2016.1210331

[52] Taşan, M., Musso, G., Hao, T., Vidal, M., MacRae, C.A. and Roth, F.P. (2014) Selecting Causal Genes from Genome-Wide Association Studies via Functionally Coherent Subnetworks. *Nature Methods*, **12**, 154-159. https://doi.org/10.1038/nmeth.3215

[53] Chopra, S., Foltz, W.D., Milosevic, M.F., Toi, A., Bristow, R.G., Ménard, C., *et al*. (2009) Comparing Oxygen-Sensitive MRI (BOLD R2) with Oxygen Electrode Measurements: A Pilot Study in Men with Prostate Cancer. *International Journal of Radiation Biology*, **85**, 805-813. https://doi.org/10.1080/09553000903043059

[54] Robinson, D., Van Allen, E.M., Wu, Y., Schultz, N., Lonigro, R.J., Mosquera, J., *et al*. (2015) Integrative Clinical Genomics of Advanced Prostate Cancer. *Cell*, **161**, 1215-1228. https://doi.org/10.1016/j.cell.2015.05.001

[55] Abida, W., Cyrta, J., Heller, G., Prandi, D., Armenia, J., Coleman, I., *et al*. (2019) Genomic Correlates of Clinical Outcome in Advanced Prostate Cancer. *Proceedings of the National Academy of Sciences*, **116**, 11428-11436. https://doi.org/10.1073/pnas.1902651116

[56] Pope, S.D. and Medzhitov, R. (2018) Emerging Principles of Gene Expression Programs and Their Regulation. *Molecular Cell*, **71**, 389-397. https://doi.org/10.1016/j.molcel.2018.07.017

[57] Brouwer, I. and Lenstra, T.L. (2019) Visualizing Transcription: Key to Understanding Gene Expression Dynamics. *Current Opinion in Chemical Biology*, **51**, 122-129. https://doi.org/10.1016/j.cbpa.2019.05.031

[58] Eke, I., Bylicky, M.A., Sandfort, V., Chopra, S., Martello, S., Graves, E.E., *et al*. (2021) The LncRNAs LINC00261 and LINC00665 Are Upregulated in Long-Term Prostate Cancer Adaptation after Radiotherapy. *Molecular Therapy-Nucleic Acids*, **24**, 175-187. https://doi.org/10.1016/j.omtn.2021.02.024

[59] Zhao, F., Zhang, T., Wei, J., Chen, L., Liu, Z., Jin, Y., *et al*. (2024) Integrated Single-Cell Transcriptomic Analyses Identify a Novel Lineage Plasticity-Related Cancer Cell Type Involved in Prostate Cancer Progression. *eBioMedicine*, **109**, Article 105398. https://doi.org/10.1016/j.ebiom.2024.105398

[60] Chen, S., Zhu, G., Yang, Y., Wang, F., Xiao, Y., Zhang, N., *et al*. (2021) Single-Cell Analysis Reveals Transcriptomic Remodellings in Distinct Cell Types That Contribute to Human Prostate Cancer Progression. *Nature Cell Biology*, **23**,

87-98. https://doi.org/10.1038/s41556-020-00613-6

[61] Tanase, C.P., Codrici, E., Popescu, I.D., Mihai, S., Enciu, A., Necula, L.G., *et al*. (2017) Prostate Cancer Proteomics: Current Trends and Future Perspectives for Biomarker Discovery. *Oncotarget*, **8**, 18497-18512. https://doi.org/10.18632/oncotarget.14501

[62] Valdés-Mora, F. and Clark, S.J. (2014) Prostate Cancer Epigenetic Biomarkers: Next-Generation Technologies. *Oncogene*, **34**, 1609-1618. https://doi.org/10.1038/onc.2014.111

[63] Tonry, C., Finn, S., Armstrong, J. and Pennington, S.R. (2020) Clinical Proteomics for Prostate Cancer: Understanding Prostate Cancer Pathology and Protein Biomarkers for Improved Disease Management. *Clinical Proteomics*, **17**, Article No. 41. https://doi.org/10.1186/s12014-020-09305-7

[64] Katsogiannou, M., Boyer, J., Valdeolivas, A., Remy, E., Calzone, L., Audebert, S., *et al*. (2019) Integrative Proteomic and Phosphoproteomic Profiling of Prostate Cell Lines. *PLOS ONE*, **14**, e0224148. https://doi.org/10.1371/journal.pone.0224148

[65] Davalieva, K., Kostovska, I.M., Kiprijanovska, S., Markoska, K., Kubelka-Sabit, K., Filipovski, V., *et al*. (2015) Proteomics Analysis of Malignant and Benign Prostate Tissue by 2D DIGE/MS Reveals New Insights into Proteins Involved in Prostate Cancer. *The Prostate*, **75**, 1586-1600. https://doi.org/10.1002/pros.23034

[66] Launonen, K., Paakinaho, V., Sigismondo, G., Malinen, M., Sironen, R., Hartikainen, J.M., *et al*. (2021) Chromatin-directed Proteomics-Identified Network of Endogenous Androgen Receptor in Prostate Cancer Cells. *Oncogene*, **40**, 4567-4579. https://doi.org/10.1038/s41388-021-01887-2

[67] Zhang, A., Sun, H., Yan, G., Wang, P. and Wang, X. (2015) Metabolomics for Biomarker Discovery: Moving to the Clinic. *BioMed Research International*, **2015**, Article 354671. https://doi.org/10.1155/2015/354671

[68] Bansal, N., Kumar, M., Sankhwar, S.N. and Gupta, A. (2022) Relevance of Emerging Metabolomics-Based Biomarkers of Prostate Cancer: A Systematic Review. *Expert Reviews in Molecular Medicine*, **24**, e25. https://doi.org/10.1017/erm.2022.20

[69] Kumar, D., Gupta, A., Mandhani, A. and Sankhwar, S.N. (2016) NMR Spectroscopy of Filtered Serum of Prostate Cancer: A New Frontier in Metabolomics. *The Prostate*, **76**, 1106-1119. https://doi.org/10.1002/pros.23198

[70] Giunchi, F., Fiorentino, M. and Loda, M. (2019) The Metabolic Landscape of Prostate Cancer. *European Urology Oncology*, **2**, 28-36. https://doi.org/10.1016/j.euo.2018.06.010

[71] Gómez-Cebrián, N., Poveda, J.L., Pineda-Lucena, A. and Puchades-Carrasco, L. (2022) Metabolic Phenotyping in Prostate Cancer Using Multi-Omics Approaches. *Cancers*, **14**, Article 596. https://doi.org/10.3390/cancers14030596

[72] Mah, C.Y., Nassar, Z.D., Swinnen, J.V. and Butler, L.M. (2020) Lipogenic Effects of Androgen Signaling in Normal and Malignant Prostate. *Asian Journal of Urology*, **7**, 258-270. https://doi.org/10.1016/j.ajur.2019.12.003

[73] Drago, D., Andolfo, A., Mosca, E., Orro, A., Nocera, L., Cucchiara, V., *et al*. (2021) A Novel Expressed Prostatic Secretion (EPS)-Urine Metabolomic Signature for the Diagnosis of Clinically Significant Prostate Cancer. *Cancer Biology & Medicine*, **18**, 604-615. https://doi.org/10.20892/j.issn.2095-3941.2020.0617

[74] McCann, S.M., Jiang, Y., Fan, X., Wang, J., Antic, T., Prior, F., *et al*. (2016) Quantitative Multiparametric MRI Features and *PTEN* Expression of Peripheral Zone Prostate Cancer: A Pilot Study. *American Journal of Roentgenology*, **206**, 559-565. https://doi.org/10.2214/ajr.15.14967

[75] Dinis Fernandes, C., Schaap, A., Kant, J., van Houdt, P., Wijkstra, H., Bekers, E., *et al*. (2023) Radiogenomics Analysis Linking Multiparametric MRI and Transcriptomics in Prostate Cancer. *Cancers*, **15**, Article 3074. https://doi.org/10.3390/cancers15123074

[76] Zhang, G., Zhang, Z., Pei, Y., Hu, W., Xue, Y., Ning, R., *et al*. (2023) Biological and Clinical Significance of Radiomics Features Obtained from Magnetic Resonance Imaging Preceding Pre-Carbon Ion Radiotherapy in Prostate Cancer Based on Radiometabolomics. *Frontiers in Endocrinology*, **14**, Article 1272806. https://doi.org/10.3389/fendo.2023.1272806

[77] Yip, S.S.F. and Aerts, H.J.W.L. (2016) Applications and Limitations of Radiomics. *Physics in Medicine and Biology*, **61**, R150-R166. https://doi.org/10.1088/0031-9155/61/13/r150

[78] Integrative HMP (iHMP) Research Network Consortium (2014) The Integrative Human Microbiome Project: Dynamic Analysis of Microbiome-Host Omics Profiles during Periods of Human Health and Disease. *Cell Host & Microbe*, **16**, 276-289. https://doi.org/10.1016/j.chom.2014.08.014

[79] Wilkinson, M.D., Dumontier, M., Aalbersberg, I.J., Appleton, G., Axton, M., Baak, A., *et al*. (2016) The FAIR Guiding Principles for Scientific Data Management and Stewardship. *Scientific Data*, **3**, Article No. 160018. https://doi.org/10.1038/sdata.2016.18

[80] Tarazona, S., Arzalluz-Luque, A. and Conesa, A. (2021) Undisclosed, Unmet and Neglected Challenges in Multi-Omics Studies. *Nature Computational Science*, **1**, 395-402. https://doi.org/10.1038/s43588-021-00086-z

[81] Subramanian, I., Verma, S., Kumar, S., Jere, A. and Anamika, K. (2020) Multi-Omics Data Integration, Interpretation,

and Its Application. *Bioinformatics and Biology Insights*, **14**. https://doi.org/10.1177/1177932219899051

[82] Hong, M., Pawitan, Y., Magnusson, P.K.E. and Prince, J.A. (2009) Strategies and Issues in the Detection of Pathway Enrichment in Genome-Wide Association Studies. *Human Genetics*, **126**, 289-301. https://doi.org/10.1007/s00439-009-0676-z

[83] Canzler, S. and Hackermüller, J. (2020) Multigsea: A Gsea-Based Pathway Enrichment Analysis for Multi-Omics Data. *BMC Bioinformatics*, **21**, Article No. 561. https://doi.org/10.1186/s12859-020-03910-x

[84] van Karnebeek, C.D.M., Wortmann, S.B., Tarailo-Graovac, M., Langeveld, M., Ferreira, C.R., van de Kamp, J.M., *et al*. (2018) The Role of the Clinician in the Multi-Omics Era: Are You Ready? *Journal of Inherited Metabolic Disease*, **41**, 571-582. https://doi.org/10.1007/s10545-017-0128-1

[85] Lee, J., Hyeon, D.Y. and Hwang, D. (2020) Single-Cell Multiomics: Technologies and Data Analysis Methods. *Experimental & Molecular Medicine*, **52**, 1428-1442. https://doi.org/10.1038/s12276-020-0420-2

[86] Meier, M.J., Harrill, J., Johnson, K., Thomas, R.S., Tong, W., Rager, J.E., *et al*. (2024) Progress in Toxicogenomics to Protect Human Health. *Nature Reviews Genetics*, **26**, 105-122. https://doi.org/10.1038/s41576-024-00767-1