Opinion

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Developing Effective and Well-Tolerated Alternatives to BCG

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Description

Intravesical immunotherapy with Bacillus Calmette-Guérin has been the standard of care for patients with high-risk non non–muscle invasive bladder cancer for over four decades. Despite its success as a cancer immunotherapy, disease recurrence and progression remain common. Current efforts are focused on developing effective and well-tolerated alternatives to BCG and salvage bladder preservation therapies after BCG has failed. The focus of this review is to synthesize our current understanding of the molecular biology and tumor immune microenvironment of NMIBC to provide rationale for existing and emerging therapeutic targets. We highlight recent and ongoing clinical trials and define the current treatment landscape, challenges, and future directions of salvage treatment. Combination regimens that are rationally designed will be needed to make meaningful therapeutic advancements. Investigations into the molecular underpinnings of NMIBC are leading to the emergence of predictive molecular biomarkers that provide greater insight into the clinical heterogeneity of NMIBC and enable us to identify drivers of treatment resistance and new therapeutic targets.

Basic Histopathological Features of Novel Ameloblastoma

Ameloblastoma is the most common odontogenic epithelial tumour. This often results in an enlarged jaw and facial deformities. Although it is a benign tumour, it has aggressive local growth and a high recurrence rate after surgery. It can also become malignant or metastasis to distant sites. Many risk factors contribute to the development of ameloblastoma, such as chronic inflammation, exposure to various chemicals, human papillomavirus infections, malnutrition, protein or mineral deficiencies, poor dental health, and individual genetic polymorphisms. A categorization of ameloblastoma in 2017 included conventional ameloblastoma, unicystic ameloblastoma, extra osseous/peripheral ameloblastoma, and metastasizing (malignant) ameloblastoma. The classification merges the solid/polycystic and desmoplastic types into conventional ameloblastomas. Unicystic ameloblastomas include intraluminal, luminal, and mural variants. In 2022, the World Health Organization updated the classification of ameloblastoma to include adenoid ameloblastoma, which is a newly-discovered form. Basic histopathological features of this novel ameloblastoma include ameloblastoma-like components, tubular structures, cribriform structures, and helical cell aggregates, with or without dentin-like structures. Most RPS is incidental findings in the radiological work-up of unrelated symptoms, and tumors can grow to a major size before causing symptoms. If benign soft tissue tumors are largely predominant in the other parts of the body, malignant tumors are four times more frequent than benign lesions in the retroperitoneum, thus requiring a rapid diagnostic strategy. After appropriate imaging, the standard diagnostic approach for RPS requires multiple image-guided, percutaneous coaxial core needle biopsies with 14–16G needles, preferably by retroperitoneal route. The biopsy should be performed by a radiologist after discussion with expert surgeons or after a multidisciplinary tumor board in a reference center. Image guidance may help identify solid tumor areas in case of necrotic or cystic lesions. Tumor biopsies should be rapidly fixed in 4% buffered formalin and subsequently embedded in paraffin blocks. Middle-throughput RNA and DNA analyses can be consistently performed with FFPE material. The collection of fresh frozen tissue may enable further molecular analyses but is not mandatory as first approach for the diagnosis of most retroperitoneal sarcomas. A histological diagnosis is mandatory to eliminate benign tumors and other malignancies distinct from RPS that can constitute differential diagnoses. Moreover, the precise identification of RPS subtype is mandatory as the pathological subtype can influence prognosis and guide further therapeutic strategies, such as surgical approaches and systemic treatments.

Different Knowledge Elements to Novel Innovations

To shed more light on the relationship between expertise diversity and team innovation performance, we build on and extend the team diversity literature by simplifying and disentangling the construct of expertise diversity into different subdimensions. We conceptualize multiplicity in expertise as a potential for innovation and define it as the no redundant presence or absence of expertise in contrast to the diversity literature, which conceptualizes diversity as distribution, including redundant expertise. Multiplicity in expertise leads to positive team outcomes because it represents a sufficient condition for the combination of different knowledge elements

to novel innovations. This definition allows us to distinguish it from three conditions facilitating or impairing the integration of multiplicity in expertise. These conditions are firstly, overlap in expertise. If individual members have overlapping knowledge and skills, the multiplicity of expertise can be better integrated. Secondly, we identify disparity in status as the diversity in status among team members. It impairs the positive potential of multiplicity in expertise by making it more difficult to integrate diverse knowledge and skills. Finally, we identify the use of automation technology as an inhibitor for integrating multiplicity in expertise. To operationalize the use of automation technology, we exploit that teams in our research context can use a certain automation technology called gene synthesis. Altogether, we pose the following research questions: How does multiplicity in expertise relate to team performance? How is this relationship moderated by overlap in expertise, disparity in status, and the use of gene synthesis? We formulate hypotheses on the effects of the constructs and test them in the research context of scientific teams in molecular biology, more precisely the part of that field that produces and exchanges genetic material in the form of so-called plasmids. Here, biologists create new genetic material, thereby exchanging and reusing available material. They codify the genetic material in the form of plasmids, which exist independently of chromosomes. This independence makes it easy to redesign and transfer them between organisms and therefore an open exchange system has emerged. The activity of plasmid creation and exchange covers multiple fields, such as synthetic biology, virology, and cell biology. The context of plasmid creation and exchange in molecular biology is well suited to our research. Most fundamentally, as in most scientific fields, teamwork is common. Rich data on teams and their outcomes are available because molecular biologists usually deposit their plasmids (i.e., the actual genetic material) in public repositories, which enable the sharing with other researchers. In parallel, they describe the genetic material in scientific publications. Thus, we can capture team compositions by extracting information on the authors of these publications. We also can compare two different performance measures: citations of the articles describing the plasmids and the number of plasmids ordered from the repository. The data also allow us to identify whether teams have used the automation technology of gene synthesis.