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0610/62

Paper 6 Alternative to Practical

May/June 2024

1 hour

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PAPER 6

COMPLETE WALKTHROUGH



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The receptors of the TNFRSF TNFRs are of overwhelming importance in the regulation of the immune system but are also involved in the induction of apoptotic cell death or cell survival and proliferation making them excellent therapeutic targets for cancer but also other diseases TNFRSF members provide crucial co stimulatory signals to many if not all immune effector cells Each co stimulatory TNFR has a distinct expression profile and a unique functional impact on various types of cells and at different stages of the immune response For example the two receptors of TNF TNF receptor 1 TNFR1 and TNF receptor 2 TNFR2 regulate the interaction of the various types of immune cells and also the interplay of the latter with practically any type of non hematopoietic cells CD40 stimulates antigen presenting cells CD27 OX40 41BB GITR HVEM and RANK costimulate T cells BCMA TACI and BaffR regulate B cell maturation CD95 and the two death receptors of TRAIL contribute to tumor surveillance and Fn14 EDAR and XEDAR have been implicated in tissue regeneration and development Correspondingly exploiting TNFR mediated signaling for the therapy of cancer but also of non cancerous diseases is a major field of interest A further application of TNFRSF signaling is the incorporation of the intracellular co stimulatory domain of a TNFRSF receptor into so called Chimeric Antigen Receptor CAR constructs for CAR T cell therapy the most prominent example of which is the 4 1BB co stimulatory domain included in the clinically approved product Kymriah The goal of this research topic is to provide concise overview of the recent advances in our understanding of agonists targeting TNFRSF and their potential therapeutic use in particular in cancers The focus of the series of research and review articles includes but is not limited to the biology of TNFRSF receptors in distinct immune cell populations structure function relationship of TNFRSF agonists current preclinical and clinical knowledge of co stimulatory TNFR agonists opportunities for next generation TNFRSF therapeutics alone or in combination with immune checkpoint molecules We encourage the submission of original research articles supported by pre clinical data Review articles will also be considered Data should consist of anti tumor activity analyses encompassing various murine or humanized mouse models assessment of TNFRSF targeting in translational ex vivo primary human tumor tissue settings or innovative single cell or spatial analysis of TNFRSF expression and association with tumor progression in patient material Submissions should not be limited to the in vitro evaluation of TNFRSF signaling We expect submissions based on

but not limited to TNFRSF signaling in shaping the immune contexture for anti tumor immunity Engaging cytotoxic TNFRSF signaling to treat cancer Engaging TNFRSF signaling in non cancerous diseases Immunobiology of TNFRSF receptors in specific immune cell populations eg regulatory T cells TNFR2 41BB TNFRSF25 dendritic cells CD40 RANK NK cells Critical aspects of TNFRSF structure function and receptor clustering Balancing agonistic strength with Fc R affinity in the context of opportunities for next generation anti TNFR antibodies with improved pharmacologic properties TNFSF based agonists with conditional or constitutive agonism Potential of simultaneous blockade of immune checkpoint molecules and co stimulation of the TNFRSF in improving anti tumor immunity Bispecific TNFR agonists anti TNF agents in cancer immunotherapy Prominence and key features of TNFRSF members 4 1BB OX40 CD27 CD40 HVEM and GITR as co stimulatory domains in CAR T cell therapy Current preclinical and clinical knowledge of co stimulatory TNFR antibodies

Topic Editor Nata a Obermajer is a full time employee and shareholder of Janssen R The University of W rzburg has filed patent applications for TNFR2 Fn14 and CD40 agonists and bispecific anti TNFR antibody formats with conditional activity with Dr Harald Wajant as co inventor The University of W rzburg receives funding from Dualyx NV for the development of TNFR2 agonists

New Publications of the U.S. Geological Survey ,1995 [New Publications of the Geological Survey](#) Geological Survey (U.S.),1995 **Key British Enterprises** ,1997 **Cape peninsula** South Africa. Department of Posts and Telecommunications,1995 *The Acute and Long-Term Impact of COVID-19 on Mental Health of Children and Adolescents* Kai Yuan,Yanping Bao,Yue Leng,Xiaoyu Li,2023-11-13 The coronavirus disease 2019 COVID 19 epidemic has dramatically spread throughout the world which has also caused mental health problems among the public especially vulnerable groups like children and adolescents As a traumatic event the outbreak of COVID 19 might increase the prevalence of a series of mental health problems in children and adolescents probably due to social distancing school closures as well as separation from parents and home quarantine The continuing spreading of COVID 19 infection as well as vaccine uptake strategies quarantine policies and health services during post epidemic era may also have a long lasting side effect on children and adolescents Children and adolescents are in critical periods of neurodevelopment and once they develop mental health problems the long lasting negative influence might span across their lifetime Moreover long term multisystem sequelae including neurological and psychiatric systems of COVID 19 infection in children also compromise the development of physical and mental wellbeing in adulthood Though there have been several studies on mental health consequences and long term impact on the mental health of children and adolescents caused by COVID 19 there is still limited data and more comprehensive studies are needed on this important topic

Advances in Molecular Pathology Felipe Simon,Carmelo Bernabeu,2023-04-24 The present work corresponds to a compilation of independent contributions in the fields of endocrinology immunity cancer neurobiology and myology Revision of current advances as well as novel findings in the form of original articles are presented in a balanced fashion The book has been divided into three sections in line with

the main subject Molecular pathology of immune inflammatory and hemostatic disorders Molecular pathology of endocrine and muscular disorders and Molecular pathology of cancer determinants and potential therapies In the first section contributing authors take the reader through the molecular pathology of immune responses inflammation and hemostasis by collating an update on systemic autoimmune diseases the therapeutic potential of statins in hemostasis the effects of adrenergic stimulation on coagulation the emerging field of physical burnout due to the mobility restrictions in response to the 2020 SARS CoV 2 pandemic imposed worldwide and the success of community oriented muscular kinesic rehabilitation The second section presents engaging results from a survey of iodine intake through the diet of pregnant females an appraisal of the neuroprotective effect of dexmedetomidine novel evidence on muscle physiopathology describing the upregulation of CCL5 RANTES during cholestatic liver disease the fibrotic response emerging in response to cholic and deoxycholic acids and the altering effects of bile acids in autophagy and mitogenesis In the third section a comprehensive revision of cancer literature is offered with an emphasis on melanoma myeloid derived suppressor cells microRNA based diagnostic approaches and new avenues for cancer immunotherapy Altogether these individual contributions offer a comprehensive and up to date outlook of the current state in the field of molecular pathology Chapter 14 is available open access under a Creative Commons Attribution 4 0 International License via link [springer.com](https://www.springer.com) *Understanding, assessing, and guiding adaptations in public health and health systems interventions: Current and future directions* Roman Aydiko Ayele,Borsika Adrienn Rabin,Catherine Battaglia,Marina McCreight,2023-07-19 **Metals Abstracts Index** ,1996 *Northern Province White & Yellow Pages* ,2000 Transkei ,1993

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