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编者按：2011 年，中国生理学会成立 85 周年之际，学会编辑出版了以王晓民理事长为主编的上下两本图书，上册为《根深叶茂 蔚然成荫——中国生理学人物记》，下册为《根深叶茂 蔚然成荫——中国生理学团队记》。从 2013 年第 3 期开始，《生理通讯》将陆续转载，以飨读者。

生理学家

吴功贤先生传略

温璋文　万 瑜


吴功贤
（1903 年-1987 年）

我虽然没能赶上做吴功贤教授的学生，但通过走访吴老当年工作过的武汉大学生物系（现已并入生命科学院）、吴老带教过的学生魏劲波教授以及吴老的女儿吴银芳、孙子邱明新等，同时翻阅一些曾经介绍过吴老先生的文章和江苏省如东县县志后，我深感历史真切，每一页都很实、很真……

吴功贤先生于 1903 年 3 月 23 日出生于江苏省如东县双甸镇郊吴家庄。1929 年 7 月从南京中央大学生物系动物学专业毕业，尔后一直从事生理学教学与科研工作，直到 1983 年退休，历时半个多世纪，真可称我国老一辈生理学家。

吴先生从南京“中央大学”毕业后，留校在生物系任助教；1935 年转至北平私立中国大学生物系任教；1936 年赴英国留学，主修动物学，1938 年获伦敦大学 Ph.D 后决定回国工作，到“中央大学”生物系任教授，1947 年至 1949 年兼任该校人事室主任；1949 年到无锡江南大学农学院任教授，次年应江西南昌大学之邀到生物系任教授和系主任，同时兼中南军区医学院生理教研室主任；1953 年全国院系大调整时，由武汉大学法学院韩德培教授介绍，来武大生物系任教授，后担任动物生理教研室主任，兼湖北省生理科学会理事直到退休。

吴先生曾于 1927 年在南京加入国民革命党，1956 年在武大参加中国民主促进会，努力为国分忧。1987 年 4 月 12 日，吴功贤教授在武汉大学病故，享年 85 岁。

一、兢兢业业　教书育人

吴功贤教授在 50 多年的教学生涯中，兢兢业业、教书育人，为国家培养了大量的生命科学人才。据他的学生回忆，在武汉大学工作期间，他经历了“反右”、“四清”、“文革”等一系列的运动。由于家庭出身地主，历次运动中他都努力“销声匿迹”，埋头教学，从不张扬。他长期负责开设多门生理学及其相关课程，除了主讲动物生理学和人体生理学外，还讲授过人体解剖学、动物比较解剖学、生殖生理学以及高级神经活动生理学等课程教学。1958 年，武汉大学生物系增设“动物生理学”专业，吴功贤教授出任动物生理教研室主任，该专业设置了“比较生理学”课程，当时国内尚无先例，根本找不到动物比较生理学方面的中文教材，教学难度较大，吴先生便主动承担授课任务，通过广泛查阅资料，日夜赶写讲义，经过几轮教学实践后，于 1960 年出版了我国第一本《动物比较生理学》教材。

吴教授不仅很注重课堂“传道”，也特别注重课外“解惑”，经常利用课余时间，主动接近学生，热情介绍自己在国外的学习经历，激发同学们的学习热情。在 20 世纪五六十年

代的学生勤工俭学活动中，吴教授经常与学生一同参加劳动，还曾一起打扫猪圈、割猪饲料，以拉近教授与学生之间的距离，了解学生、感染学生、教育学生。这也是那个年代一道特殊的风景线。吴教授热爱生理学这一专业的教学工作，还体现在他对青年教师成长的特别关注，为了弥补文革对教育、对师资造成的损失，20 世纪 70 年代后期，他虽然年过古稀，仍经常到实验室，悉心指导青年教师做实验、帮助修改教案、指导学习专业英语，用他的余热关心生理学专业人才的成长。

“文化大革命”期间，生理实验室和实验仪器设备遭受浩劫，对此他十分痛心。对劫后残存的部分仪器设备他倍加爱护，每天除了进行教学和科研工作外，还主动照管生理实验室和实验仪器设备，发现仪器坏了，他常自己动手修理，生怕哪天开课时做不了实验。在那个特殊的年代里，他常常语重心长地提醒年轻老师：“生理学课以后还是要开的，一定要保护好实验室。没有实验室和实验仪器，将来怎么开课？”吴功贤教授对生理学教育事业这种炽热的情怀和敬业精神实在难能可贵！

“文化大革命”后期，武汉大学生物系新辟药学专业。为了开出适合药学专业的人体解剖生理学和药理学课程，已是七十开外的吴教授，毫不犹豫又潜心于药学专业的教学工作，他既当教师又当实验员，除了负责编写这两门课程的讲义外，还亲自解剖尸体，工作一丝不苟。据他的学生回忆，药学专业开课的第一年冬天，有次他在实验室做尸体解剖，下班时其他同志没留意吴教授还在做尸解，将实验室门反锁了……幸亏晚饭后有位年轻老师去实验室看标本，这才发现吴老师被锁在里面做解剖，早已错过了下班时间。可见年逾古稀的吴教授，工作起来仍然是废寝忘食。

二、脚踏实地　开展科研

吴先生早年在南京“中央大学”生物系主要研究大脑皮层细胞的生长发育，其论文有《白鼠大脑皮质细胞生长的研究》（中国动物学杂志，1935 年，第一卷，68-75 页）和《大脑皮层细胞内高尔基体之变迁》（中国科学社生物研究所会议报告，1935）。因对神经生理研究成绩突出，获 200 英镑奖学金，于 1936 年赴英国留学。

留英期间，他在伦敦大学从事蚯蚓消化道的生理及药理研究，观察乙酰胆碱（ACh）、肾上腺素、毒扁豆碱、麦角毒素和阿托品等对蚯蚓消化道的作用。发现蚯蚓消化道各部分均对 ACh 敏感，尤以嗉囊和砂囊对 ACh 最为敏感，而肾上腺素、组胺具有增强 ACh 的作用，阿托品则可消除 ACh 的影响，显示 ACh 存在“毒蕈碱作用”（muscarinicaction）。但在此之前，另有研究发现大剂量尼古丁可消除 ACh 对蚂蟥背部肌条的作用，称之 ACh“尼古丁作用”（nicotinicaction）。他的这些结果与前人的研究明显不一致。为了弄清 ACh 这些作用的不同究竟是由于物种的不同还是器官的差异所造成，吴先生又进行了环节动物肌肉生理和药理学研究。发现蚯蚓和蝎体壁肌条对 ACh 的作用与蚂蟥体壁肌和脊椎动物骨骼肌的作用相同，表现为它们对 ACh 单独作用不甚敏感，但毒扁豆碱能使肌肉对 ACh 的敏感性大大加强，尼古丁则可消除 ACh 对肌肉的作用。从而表明了 ACh 具有的“尼古丁作用”和毒蕈碱作用与物种没有关系。现在看来，这是 ACh 与其不同受体亚型相互作用的结果。他当时的这些研究结果对药理学、生理学、特别是比较生理学的发展均具有重要的价值。1939 年，英国《实验生物学杂志》发表了他的两篇相关论文，因此，他获得了伦敦大学的博士学位。

1938 年底，吴先生学成归国，到中央大学任教授，继续从事东亚蚯蚓消化道生理及药理研究，论文于 1949 年发表于中国动物学杂志。在无锡江南大学农学院任教期间，吴教授开展了家蚕产丝器官生理量度的研究，论文于 1950 年发表于中国水生生物学报。1953 年来武汉大学生物系后，因当时动物专业研究方向主攻鱼类，吴教授便根据需要，开展鱼类消化生理研究。

在科研工作中，吴教授 50 年如一日，表现出崇高的职业道德。有成绩时，他从不突出个人。有困难时，他总是自力更生，从没以老教授的身份向学校伸手要过高的条件。研究方向有变化时，他总是努力适应大局和现有条件，主动调整自己的研究课题，从蚯蚓、鱼类的消化生理到 1958 年后的鸟类生殖生理，再到 1978 年创建药学专业后，以中药为对象，研究灵芝针剂的药理、长春新碱的药理和茯苓的利尿作用；晚年，他还与武汉地质大学合作，担任地震征兆与动物行为变化的课题负责人，他不顾自己年事已高，积极投入工作，查阅有关地震与动物行为方面的文献资料，设计实验，亲自选购仪器，为我国开展动物行为与地震预测的研究劈山开道。更为可贵的是他实事求是的科学态度，在 20 世纪 50 年代末，全国各行业浮夸风盛行，为达到畜牧业高产，生理专业的学生对学校养猪场的牲猪进行甲状腺部分切除手术，以提高猪肉产量。而吴先生从生理学的角度，毫不客气质疑，“切割甲状腺后的猪长的是‘肉’还是‘水’”？当时他的话一出，就受到大会批判，尽管如此，吴先生仍然坚持自己的看法，这给同学们留下了终生难忘的记忆，1961 届毕业的学生每次聚会想到吴先生时总忘不了提起此事。

三、捧赤子心　报三春晖

1939 年-1941 年，吴功贤在中央大学（已西迁重庆）任教期间，为了对付日本飞机的空袭，保护学校和师生员工的安全，他加入到学校“防护团”，负责在日机空袭时，引领教师和学生迅速进入防空洞，并在洞口担任警戒；同时还受命“如果学校意外被炸，迅速参与指挥抢救”；此外，还负责当日机撤离时，发布解除警报……

1949 年春，新中国成立前夕，吴教授获悉女儿吴银芳加入了中国人民解放军，心中无比地高兴，专程到部队驻地看望女儿，勉励她努力为国家建功立业。

唐山大地震后，吴教授奉命担任地震征兆与动物行为变化的课题负责人（1977），他兴奋不已，预感科学的春天即将到来，特意来到人民大会堂前，摄影留念。

吴功贤教授在半个多世纪中，一直在生理学第一线执教，一贯勤勤恳恳、认认真真、严谨治学、为人师表，他永远是我们的楷模。

生理学团队

兰州大学基础医学院医学生理学与心理学研究所

兰州大学基础医学院医学生理学与心理学研究所（医学生理）是原兰州医学院生理学教研室和心理学教研室组合成立的研究所，根据专业现划分为生理室和心理室，现任所长郑天珍教授。

生理室现有人员共 9 人，正教授 3 人，副教授 1 人，讲师 5 人；其中具有博士学位 3 人，在读博士 2 人，其他人员均具有硕士学位。生理学专业是原兰州医学院第一批硕士授权点，现有硕士生导师 4 人。省高校跨世纪学术技术带头人 1 人，“333”和“555”人才各 1 人，省卫生厅学术技术带头人 1 人。

作为一门医学基础课教研室，经过几代人的努力，默默耕耘，几番风雨，几度春秋，在教学和科研上不断地走向成熟和发展。生理教研室 1978 年开始招收硕士学位研究生，自获得硕士授予权以来共培养研究生百余名，发表教学和科研论文近 200 余篇，参编教材、教学参考书、专著等 15 本，获国家级及省部级科研教学奖项 20 余项，举办了四届全国性的胃

肠电（运动）学术研讨会和四届甘肃省生理学术研讨会。

在教学工作方面，为给后继临床医学课程学习打下牢固的基础。生理人兢兢业业、一丝不苟地为数以万计的医学生讲授生理知识，主要承担全校临床医学、药学、口腔医学、预防医学、医学检验、医学影像、麻醉和护理专业等的本专科生生理学理论、实验教学任务及各专业硕士研究生教学任务，年教学时数达 2500 学时以上。近几年随着科学技术的飞速发展，生理学知识越来越丰富，为了提高教学质量，本室在实践中不断摸索，改进教学组织计划和教学方法，积极撰写教学论文。获甘肃省教学成果一等奖、二等奖、三等奖各一项。生理学课程 2003 年首批获得甘肃省精品课程。

科研工作历史及主要研究方向：

1.针刺针麻原理的研究：本项研究始于 1956 年，经历了十几年的探索，主要工作有：（1）针刺对内脏功能影响的研究；（2）针刺镇痛原理研究；（3）植物神经系统与针麻效果的关系。

2. 胃肠道平滑肌电活动的研究：自 1978 年开始，我室的重点研究工作是平滑肌的电生理研究，在国内处于领先地位。包括：（1）胃肠道电活动的规律及其机制探讨；（2）胃肠道电活动与机体代谢之间的关系；（3）胃肠道电活动与某些疾病之间的关系；（4）平滑肌电活动。

3. 离体平滑肌运动的研究：始于 1993 年，利用瞿颂义教授在美国进修学习到的离体平滑肌实验方法，建立起了一套离体平滑肌的实验方法，属国内首创。这方面的研究主要有：（1）利用离体胃肠平滑肌条，观察体内一些生理性因素和药物及疾病对胃肠运动的影响，从而为胃排空的机理、药物及疾病对胃肠运动的影响研究提供一定的理论依据；（2）观察某些药物对子宫平滑肌活动的影响及抗早孕作用的研究，为我国人口控制提供实验依据，从而响应“计划生育” 这一基本国策；（3）药物等因素对胆囊平滑肌活动的影响；（4）膀胱逼尿肌活动观察；（5）药物对气管平滑肌的调节。

4. 内分泌与代谢方面的研究：主要从事中药对肥胖及其基因表达的影响方面的研究。本研究方向 2005 年在基础医学方面首次获得国家自然科学基金的资助，获甘肃省高校科技进步二等奖 1 项。

5. 雌激素及结构类似物对心血管和内分泌代谢作用研究：近年来主持该方面相关研究课题 5 项，发表论文 40 余篇，其中 SCI 论文 12 篇，获甘肃省科技进步二等奖 1 项，甘肃省高校科技进步一等奖 1 项。

张锡钧基金

编者按：2015 年 10 月 24 日-25 日中国生理学会张锡钧基金会第十三届全国青年优秀生理学学术论文交流会在湖北武汉顺利召开。由各省生理学会推荐的 47 名参赛选手的论文参加评选，会议展示了选手们近 3 年来在生理学研究方面所取得的最新研究成果。经过专家对参评者论文和现场报告的综合评判，评出一等奖 1 名、二等奖 2 名、三等奖 3 名；最佳表达奖、最佳答辩奖、最佳图表奖各 1 名。从 2015 年第 5 期开始，《生理通讯》将陆续转载获奖者的参评论文各一篇，以飨读者。

ZBTB20 regulates nociception and pain sensation by modulating TRP channel expression in nociceptive sensory neurons

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In mammals, pain sensation is initiated by the detection of noxious stimuli through specialized transduction ion channels and receptors in nociceptive sensory neurons. Transient receptor potential (TRP) channels are the key sensory transducers that confer nociceptors distinct sensory modalities. However, the regulatory mechanisms about their expression are poorly defined. Here we show that the zinc-finger protein ZBTB20 regulates TRP channels expression in nociceptors. ZBTB20 is highly expressed in nociceptive sensory neurons of dorsal root ganglia. Disruption of ZBTB20 in nociceptors led to a marked decrease in the expression levels of TRPV1, TRPA1 and TRPM8 and the response of calcium flux and whole-cell currents evoked by their respective specific agonists. Phenotypically, the mice lacking *ZBTB20* specifically in nociceptors showed a defect in nociception and pain sensation in response to thermal, mechanical and inflammatory stimulation. Our findings point to ZBTB20 as a critical regulator of nociception and pain sensation by modulating TRP channels expression in nociceptors.

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In mammals, the perception of pain is initiated by the detection of noxious thermal, mechanical and chemical stimuli through the peripheral nerve fibres from a specialized subpopulation of primary sensory neurons, called nociceptors[1,2]. Nociceptors are highly diversified with different sensory modalities. There are two major subsets of small DRG neurons. One subset is peptidergic, which expresses receptor tyrosine kinase TrkA, the receptor of nerve growth factor, and synthesizes neuropeptides like calcitonin gene-related peptide (CGRP) and substance P. The other is nonpeptidergic, which expresses the c-Ret neurotrophin receptor, and responds to glial-derived neurotrophic factor, as well as neurturin and artemin. Most c-Ret-positive neurons are capable of binding the isolectin IB4 and express Mas-related G-protein-coupled receptors (Mrgpr)[3], and specific purinergic receptor subtypes, notably P2X3.

Nociceptors are equipped with a diverse array of ion channels that act as sensory transducer, each specialized to only respond to particular stimuli and initiate electrical activity. Among them, transient receptor potential (TRP) ion channels have emerged as a major sensory transducer family, with many members involved specifically in generating thermally and chemically evoked painsensations[4]. For example, TRPV1, TRPV2, TRPV3 and TRPV4 act as thermal receptors[5]. TRPV1 and TRPV2 channels display a temperature activation threshold of

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43 and 52℃, respectively, whereas TRPV3 and TRPV4 are activated between 25 and 35℃ (ref. 2). TRPV1 marks a population of unmyelinated, slowly conducting neurons (C-fibres) that express the neuropeptides substance P, neurokinin A and CGRP and constitute ~30-50% of all somatosensory neurons within rodent sensory ganglia[6]. As an endogenous transducer of noxious heat, TRPV1 is essential for selective modalities of pain sensation and tissue injury-induced thermal hyperalgesia[7]. TRPV2 is expressed in a subpopulation of Aδ neurons that respond to high-threshold noxious heat. Actually, TRPV3 and TRPV4 belong to 'innocuous' warmdetectors[8,9]. Furthermore, TRPM8 and TRPA1 putatively act as cold pain receptors[10,11]. TRPM8 is robustly expressed by ~15% of all somatosensory neurons encompassing mostly small-diameter, unmyelinated C-fibres, as well as a minor cohort of lightly myelinated Aδ fibres. TRPM8 is activated at cool temperatures (~26℃) and by the cooling compoundmenthol[10,12]. Mouse knockout studies have revealed that TRPM8 is required for cold sensation over a broad range of innocuous and noxious cold temperatures[13-15]. TRPA1 is largely restricted to TRPV1-positive neurons[16], and acts as a major sensor for noxious cold and plays an important role in chemonociception by serving as a detector of chemical irritants that elicit acute and inflammatory pain[6,11].

Remarkably, many TRP channels are generally expressed by nociceptors in a partially overlapping or mutually exclusive fashion. For example, TRPV1 and TRPM8 segregate into different classes of nociceptors in mouse DRG[17,18]. Therefore, nociceptors can also be distinguished according to their differential expression of ion channels that confer sensitivity to heat (TRPV1), cold (TRPM8) and a host of chemical irritants (TRPA1) (ref. 19). Precise regulation of the expression of these ion channels is crucial for their sensory role in nociception. However, the underlying mechanisms are still largely unknown.

Several transcription factors have been demonstrated to control the development and differentiation of nociceptive sensory neurons. The neuronal determination gene Neurogenin1 (*Ngn1*) is required for the formation of most nociceptors[20]. The homeobox gene *Brn3a* and the zinc-finger gene *Klf7* are required for the expression of TrkA and the survival ofnociceptors[21–23]. Runx1, a Runt domain transcription factor, controls neuronal diversification within *Ngn1*-dependent $TrkA^+$ neurons by repressing CGRP expression and coordinates the expression of many ion channels and receptors in nociceptors, including TRP class thermal receptors, Na^+-gated, ATP-gated and H^+-gated channels, the opioid receptor MOR and Mrgpr[18,24]. Furthermore, the transcription factor Tlx3 acts in combination with Runx1 to control the development of a cohort of nociceptors, thermoceptors, and pruriceptors in mice[25]. To date, the transcription factors that specifically regulate the differential expression of nociceptive TRP channels have not been identified.

Zinc-finger and BTB domain containing protein 20 (ZBTB20, also known as DPZF, HOF and Zfp288) belongs to a subfamily of zinc-finger proteins containing C2H2 Krüppel-type zinc fingers and BTB/POZ domains[26,27]. ZBTB20 is highly expressed in central nervous system and plays a critical role in hippocampal development and function[27–31], but its function in peripheral nervous system is rarely known. In the present study, we found that ZBTB20 was highly expressed in nociceptive sensory neurons in mouse DRG and

tissue-specific ablation of ZBTB20 in nociceptors led to a robust decrease both in the expression of TRPV1, TRPM8 and TRPA1 and the pain sensitivity to thermal, mechanical and inflammatory stimuli. These findings point to ZBTB20 as a novel nociceptive regulator through specifically modulating TRP channels expression in DRG.

Results

ZBTB20 is highly expressed in nociceptive sensory neurons. To characterize the developmental regulation of ZBTB20 expression in nociceptors, we first examined its expression in the developing DRG at different embryonic stages. Immunohistochemical analysis demonstrated that ZBTB20 protein was first detected in the DRG as early as embryonic day 13.5 (E13.5), and was increased by E14.5 (Supplementary Fig. 1). In the DRG of adult mice, double immunostaining showed that ZBTB20 was highly expressed in peripherin-positive small neurons, but was hardly detected in neurofilament (N200)-positive large neurons (Fig. 1a,b). To further characterize its expression in nociceptive sensory neurons, we performed double immunostaining of ZBTB20 and $Na_v1.8$, a sensory neuron-specific voltage-gated sodium channel expressed in ＞85% of nociceptors[32,33]. ZBTB20 protein was detected in the majority (75.2%±3.2%) of $Na_v1.8$-positive neurons (Fig. 1c). These data suggest that ZBTB20 is preferentially expressed in nociceptive sensory neurons, and might be involved in nociception.

Tissue-specific ablation of ZBTB20 in nociceptors. To evaluate the potential role of ZBTB20 in nociceptive neurons, we generated peripheral nociceptor-specific ZBTB20 knockout mice (hereafter referred to as PN-ZB20KO) by crossing $ZBTB20^{flox}$ mice to $Na_v1.8$-Cre transgenic mice[34]. This Cre transgenic line has the capacity to mediate Cre/LoxP recombination and gene deletion specifically in nociceptive neurons, starting from as early as E14 as demonstrated by LacZ reporter and X-Gal staining[35]. Efficient deletion of *ZBTB20* gene in the DRG of PN-ZB20KOmice was confirmed at the messenger RNA (mRNA) level by real-time RT–PCR and at the protein level by immunoblot analysis with an anti-ZBTB20 antibody 9A10 (Fig. 2a,b, and Supplementary Fig. 11). As expected, the expression of ZBTB20 was unchanged in the spinal cord or brain in PN-ZB20KO mice compared with controls (Fig. 2a). Double immunostaining showed that ZBTB20 was only detected in the minority (5.1%±0.3%) of Nav1.8-positive neurons of PN-ZB20KO mice, which was robustly decreased compared with control mice (75.2±3.2%, $P<0.01$) (Fig. 2c). These results indicated that we successfully generated tissue-specific knockout mice of ZBTB20 in nociceptors.

Normal morphogenesis of DRG neurons in PN-ZB20KO mice. Then we examined whether genetic deletion of *ZBTB20* in $Na_v1.8$-positive neurons could affect the development of DRG neurons. As shown in Supplementary Fig. 2a, the total number of neurons in the lumbar 4 (L4) DRG was similar between adult PNZB20KO and control mice. Moreover, percentages of peripherin-positive small neurons (62.7±2.4% in control mice versus 61.3%±2.0% in PN-ZB20KO mice) and neurofilament-positive large neurons (31.2± 2.2% in control mice versus 33.2±2.5% in PN-ZB20KO mice) were almost the same as those of controls (Supplementary Fig. 2b), showing that the generation of the two major components of DRG neurons is normal in PN-ZB20KO mice.

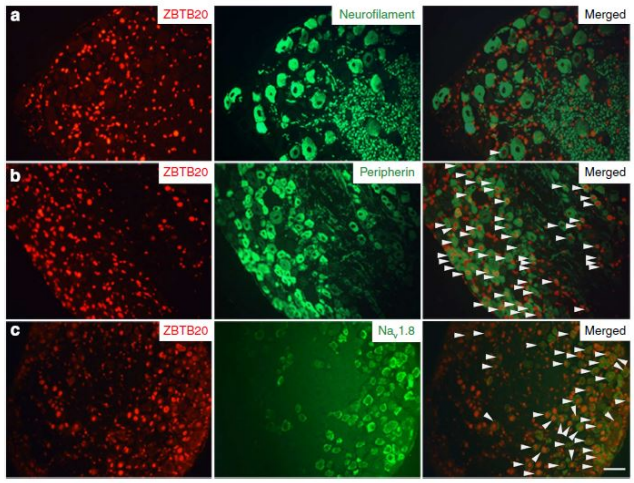

Figure 1 | ZBTB20 expression in the adult DRG. (a–c) Double immunofluorescent staining showed ZBTB20 expression was undetected in large neurofilament-positive neurons **(a)**, but present in most small peripherin-positive neurons **(b)** and $Na_v1.8$-positive neurons **(c)**. Double-labelled neurons are indicated by arrowheads. (Scale bar, 50 μm.)

We further investigated two major subsets of small DRG neurons by immunostaining or *in situ* hybridization. In the DRG sections from L4 of PN-ZB20KO mice, IB4-binding non-peptidergic neurons (29.6±2.8% in control mice versus 27.7±3.0% in PN-ZB20KO mice) and CGRP-expressing peptidergic neurons (23.2±2.7% in control mice versus 24.4±3.1% in PN-ZB20KO mice) were present at normal levels (Fig. 3a). Similarly, percentages of TrkA-positive neurons (30.2±3.1% in control mice versus 28.8±2.9% in PN-ZB20KO mice) and Ret-positive neurons (65.4±5.2% in control mice versus 67.7±5.6% in PN-ZB20KO mice) were not significantly different between the two groups (Fig. 3b). These data indicated that morphogenesis of DRG neurons was largely normal in PN-ZB20KO mice.

The gene deletion mediated by $Na_v1.8$-Cre occurs at E14 in small-diameter neurons of DRG[35], a little lagging behind their early expression of ZBTB20 at E13.5, thus we reasoned that PNZB20KO mice might not reflect the function of ZBTB20 in the early stage of neuronal morphogenesis in DRG. To exclude this possibility, we generated another conditional knockout mice lacking ZBTB20 in nervous system (hereafter NS-ZB20KO) using the Nestin-Cre transgenic mice, which mediates conditional gene deletion by E11 (ref. 36). In the L4 DRG of adult NS-ZB20KO mice, the total number of neurons (4,876±182 in control mice versus 4,754±193 in NS-ZB20KO mice), IB4-binding nonpeptidergic neurons (27.4%±2.5% in control mice versus 30.1±3.2% in NS-ZB20KO mice) and CGRP-expressing peptidergic neurons (24.4±2.8% in control mice versus 22.1±2.6% in NS-ZB20KO mice) were present at normal levels (Supplementary Figs 3 and 4). Furthermore, percentages of TrkA-positive neurons (28.4±2.0% in control mice versus 30.5±2.3% in NS-ZB20KO mice) and Ret-positive neurons (66.4±4.3% in control mice versus 65.3±4.5% in NS-ZB20KO mice) were almost the same as those of controls (Supplementary Fig. 5). Taken together, our results suggest ZBTB20 is dispensable for the morphogenesis of DRG neurons.

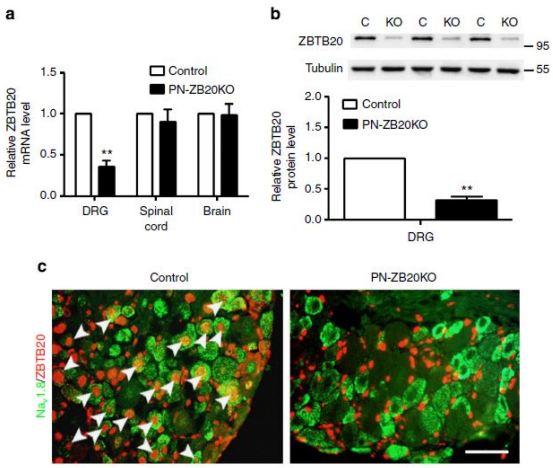

Figure 2 | Generation of PN-ZB20KO mice. **(a)** Quantitative RT–PCR analysis for ZBTB20 mRNA in DRG, spinal cord and brain from control andPN-ZB20KO mice. The RT–PCR was performed twice (n=6, $^{**}P<0.01$ versus control, Student's t-test). **(b)**Western blot analysis for ZBTB20 expression in DRG from control and PN-ZB20KO mice. C, control. KO:PN-ZB20KO (n=6, $^{**}P < 0.01$ versus control, Student's t-test). Full-size blots are shown in Supplementary Fig. 11. **(c)** Efficient and specific deletion of ZBTB20 in $Na_v1.8$-positive neurons demonstrated by double immunofluorescence staining of ZTBT20 (red) and $Na_v1.8$ (green). Double-labelled neurons are marked by arrowhead. (Scale bar, 50 μm) Values are the mean±s.e.m.

Altered TRP channels expression in DRG of PN-ZB20KO mice. The expression of high-threshold ion channels defines the specialized peripheral-receptive properties of nociceptor subclasses. To determine if ZBTB20 is required for the specification of different transduction phenotypes, we analysed the expression of nociceptive ion channels and sensory receptors in PN-ZB20KO. *In situ* hybridization showed that the percentage of TRPV1-positiveneurons in lumbar DRG was decreased from 34.2±4.1% in control mice to 17.5±2.8% in PN-ZB20KO mice, and the percentage of TRPA1-positive neurons also decreased from 30.5±3.4% to 14.2±1.9% (Fig. 4). The percentage of TRPM8-positive neurons was not significantly affected in the DRG of PN-ZB20KO mice (13.8±1.7% versus 12.6±1.5%), but their signal intensity ofTRPM8 mRNA was significantly decreased compared with control. Other nociceptive ion channels and sensory receptors, including TRPV2, P2X3, $Na_v1.7$, $Na_v1.8$, $Na_v1.9$ and Mrgpr members (Mrgprd, Mrgpr4 and Mrgpr5), did not show significant difference by *in situ* hybridization between control and PNZB20KO mice (Fig. 4, and Supplementary Fig. 6). Furthermore, immunostaining also demonstrated that ZBTB20 deficiency led to a dramatic decrease in the percentage of both TRPV1 neurons and TRPA1 neurons in adult DRG (Fig. 5a,b). Despite the unaffected percentage of total TRPM8 neurons in PN-ZB20KO DRG, their percentage of TRPM8 high-positive neurons, together with TRPV1 high-positive neurons, was robustly reduced compared with control group. Western blot analysis showed that TRPV1, TRPA1 andTRPM8 protein levels were significantly decreased in the DRG of PN-ZB20KO mice (Fig. 5c, and Supplementary Fig. 12). Despite these alterations of these TRP channels, the expression of Runx1, which regulates a large cohort of ion channels and receptors[18], was not affected in the DRG neurons by the disruption of ZBTB20 (Fig. 4). Taken together, these results suggest that ZBTB20 may regulate a subset of TRP channels in nociceptors in a Runx1-independent manner. Double immunohistochemical staining revealed that ZBTB20 protein was detected in the majority of adult TRPV1-positive, TRPA1-positive or TRPM8-positive DRG neurons in wild-type mice (Fig. 5d), suggesting that ZBTB20 may regulate the expression of TRPV1, TRPA1 and TRPM8 in a cell-autonomous manner.

To explore the mechanisms by which ZBTB20 regulates the expression of these TRP genes, we examined the association of ZBTB20 protein with their promoters individually by chromatin immunoprecipitation (ChIP). ChIP assays were performed with antibodies against ZBTB20, acetylated histone 3 (positive control) or control immunoglobulin G as negative control of chromatin recovery, and the recovered chromatin DNA was subjected to PCR analysis. As shown in Supplementary Fig. 7, ZBTB20 did not bind to the promoters of *TRPV1*, *TRPA1* or *TRPM8* genes. These results suggest that ZBTB20 most likely regulates the expression of these channels by indirect mechanisms.

Decreased calcium influx of TRP channels in PN-ZB20KO DRG. To assess the electrophysiological properties of TRPV1, TRPA1 and TRPM8 channels in PN-ZB20KO nociceptors, we first measured calcium fluxes of primary adult DRG neurons in response to the stimulation of 1 μM capsaicin (an agonist of TRPV1)[7], 100 μM mustard oil (MO, an agonist of TRPA1)[11] and 250 μM menthol (an agonist of TRPM8) (ref. 14), respectively. About 42% (76/182) of recorded control DRG neurons showed capsaicin-evoked increase of $[Ca2^{+}]_i$, while there was only 21% (39/186) in PN-ZB20KO DRG neurons (Fig. 6a). In the responded DRG neurons, the amplitude of the capsaicin-evoked responses was diminished by about 65% in PN-ZB20KO mice compared with control counterpart (Fig. 6b,c). We observed similar phenomenon in PN-ZB20KO DRG neurons when neurons were stimulated by 100 μM MO (Fig. 6d–f). Furthermore, about 8.6% (23/266) of recorded DRG neurons showed menthol-evoked increase of $[Ca2^{+}]_i$ in control mice. However, it was only 2.7% (7/258) in PN-ZB20KO mice (Fig. 6g). In the responded DRG neurons, the amplitude of the menthol-evoked responses was diminished by about 55% in PN-ZB20KO mice compared with that of control neurons (Fig. 6h,i).

Decreased currents of TRP channels in PN-ZB20KO DRG. Considering TRPV1, TRPA1 and TRPM8 proteins are channels and calcium-imaging data are not sufficient to prove the function of these TRP channels, we further investigated the function of these channels by patch clamp. Whole-cell patch-clamp recordings from acutely dissociated small and medium DRG neurons have been performed in voltage-clamp mode at a holding potential of -70 mV. Typical 1 μM capsaicin-evoked inward TRPV1 currents, 100 μM MO-evoked inward TRPA1 currents and 250 μM menthol-evoked inward TRPM8 currents have been represented as traces in Fig. 7a,c,e. Average TRPV1, TRPA1 and TRPM8 currents densities (pA pF^{-1}) have been plotted in Fig. 7b,d,f. A significant decrease in current density was observed in DRG neurons of PN-ZB20KO mice. TRPV1, TRPA1 and TRPM8 currents in DRG neurons significantly decreased from -53.0±3.1 pA pF^{-1}, -18.1±0.9 pA pF^{-1} and -14.6±0.8 pA pF^{-1} in control mice to -22.4±0.7 pA pF^{-1} ($P<0.01$), -6.3±0.6 pA pF^{-1} ($P<0.01$) and -5.2±0.5 pA PF^{-1} ($P<0.01$) in PN-ZB20KO mice, respectively. In other words, TRPV1, TRPA1 and TRPM8 currents in DRG neurons of PN-ZB20KO mice decreased 57.8%, 65.3% and 64.7%, respectively.

Deficient nociception and pain sensation in PN-ZB20KO mice. To investigate whether the molecular defects in PN-ZB20KO DRG are accompanied by alterations in behavioural responses to noxious stimuli, we assayed acute responses to thermal and mechanical stimuli, as well as

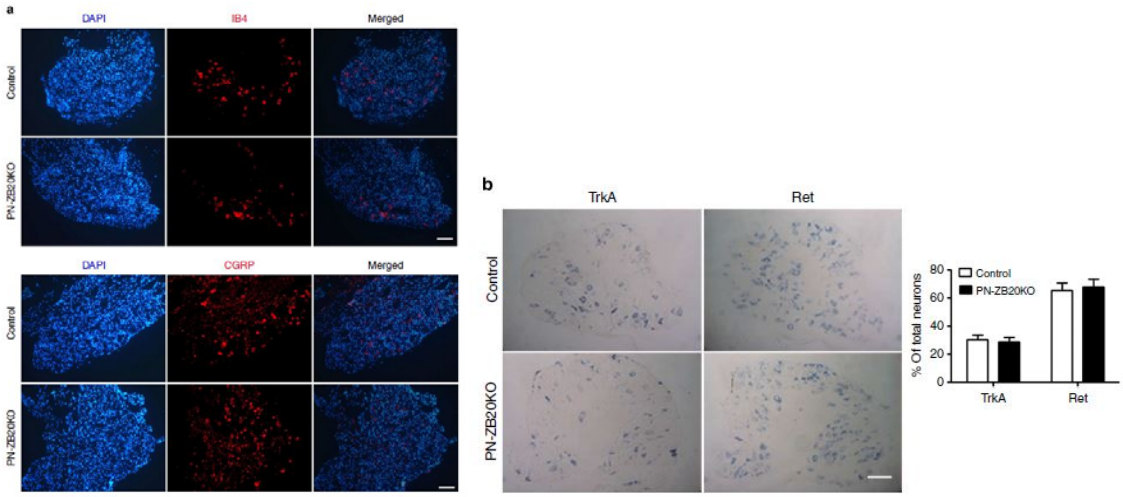

Figure 3 | Normal morphogenesis of DRG neurons in PN-ZB20KO mice. (a) DRG sections were labelled with lectin IB4-biotin or anti-CGRP antibody. IB4-binding nonpeptidergic neurons and CGRP-expressing peptidergic neurons were present at normal levels in DRG of PN-ZB20KO mice (Scale bar, 100 μm). **(b)** *In situ* hybridization performed with TrkA and Ret probes, and the numbers of neurons that express these markers were not significantly different between the two groups (Scale bar, 100 μm). About 9-12 DRG sections per animal (three animals of each genotype) were analysed. Data were analysed by Student's *t*-test. Values are the mean±s.e.m.

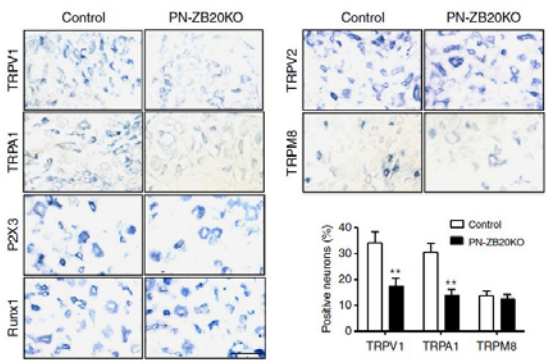

Figure 4 | TRP channel mRNA expression is decreased in DRG neurons from PN-ZB20KO mice. *In situ* hybridization performed with TRPV1, TRPA1, TRPM8 or other probes (Scale bar, 50 μm). The percentage of TRPV1-positive or TRPA1-positive neurons is significantly decreased ($^{**}P < 0.01$ versus control, Student's *t*-test). Although the percentage of TRPM8-positive neurons was not significantly changed in the DRG of PN-ZB20KO mice, the signal intensity was significantly weaker than control. About 9-12 DRG sections per animal (three animals of each genotype) were analysed $^{**}P < 0.01$ versus control. Values are the mean ± s.e.m.

inflammatory pain sensitivity. PNZB20KO mice were healthy, fertile and apparently normal. They showed no obvious differences from controls in appearance and spontaneous behaviour. Motor function was tested by rotarod studies and beam walking, and there were no significant differences in the time spent on the rod (Fig. 8a) or the number of foot slips on trail of beam walking (Supplementary Fig. 8) between control and PN-ZB20KO mice.

In the hot plate, the paw was heated by contact with a hot metal surface. PN-ZB20KO mice had normal withdrawal latencies at temperatures 50 ℃, but had significantly longer withdrawal latencies than wild-type littermates at temperatures 52.5 and 55℃ (Fig. 8b). Since ZBTB20 is required for nociception in response to thermal stimuli, we inquired whether knock out of ZBTB20 in nervous system resulted in more severe deficiency in the hot plate test. Expectedly, withdrawal latencies of

NS-ZB20KO mice were extended further than PN-ZB20KO mice at temperatures 52.5 and 55℃ (Supplementary Fig. 9). In the tail immersion test, the distal portion of the tail was immersed in a heated bath, and the time to tail flick was recorded. PN-ZB20KOmice exhibited normal latencies at ＜ 50 ℃ , but significantly longer response latencies than wild-type mice at temperatures ≥50℃ (Fig. 8c). Together, these results show that PN-ZB20KO mice display robust deficits in thermally evoked pain-related behaviour.

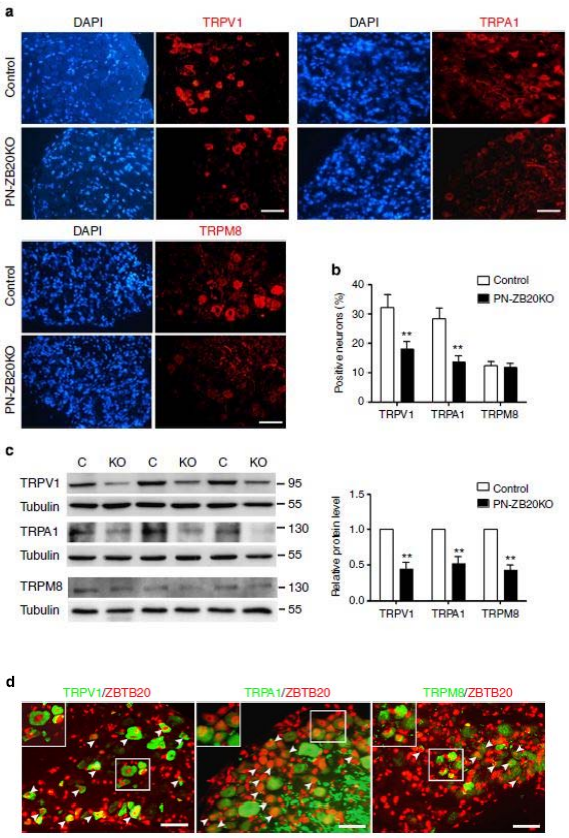

Figure 5 | Decreased expression of pain-associated channels or receptors in the DRG of PN-ZB20KO mice. (a) DRG sections of PN-ZB20KO and control mice were labelled with anti-TRPV1, anti-TRPA1 or anti-TRPM8 antibodies. **(b)** The proportion of TRPV1-expressing or TRPA1-expressing neurons was significantly decreased in PN-ZB20KO mice ($^{**}P<0.01$ versus control, Student's *t*-test). Although the percentage of TRPM8-positive neurons was not significantly changed in the DRG of PN-ZB20KO mice, the fluorescence intensity was significantly weaker than control. Four to seven independent L4 DRG were used for each counting. (Scale bar, 50 μm). **(c)** Western blot analysis showed that TRPV1, TRPA1 and TRPM8 protein levels were significantly decreased in the DRG of PN-ZB20KO mice. Full-size blots are shown in Supplementary Fig. 12. C, control mice. KO:PN-ZB20KO mice (n=6;$^{**}P<0.01$ versus control, Student's *t*-test). **(d)** Double labelling of ZBTB20 protein (red) and TRPV1 (green), TRPA1 (green) or TRPM8 (green) on adult wild-type DRG sections. Note that ZBTB20 was expressed in the majority of neurons expressing TRPV1, TRPA1 or TRPM8 (green). Double-labelled neurons are marked by arrowhead. (Scale bar, 50 μm). Values are the mean±s.e.m.

Given that a previous study showed significant sex-related differences on cold sensitivity[37], we used male mice in two-plate choice test and cold plate test. Two-plate choice test was used to determine temperature preference of animals or detection of particular temperature ranges[13]. Cold plate (0℃) test was used to determine nocifensive behaviours response to noxioustemperature[11]. In the two-plate choice test, control and PN-ZB20KO mice spent approximately equal time on both plates when both plate surfaces were held at 30℃ (Fig. 8d). When the temperature of one plate was reduced, control mice showed a clear preference for the 30℃ side. PN-ZB20KO mice showed reduced avoidance of the cooler side when the temperature is between 25 and 15℃. However, PN-ZB20KO mice displayed normal preference for 30℃ side when the other side dropped below 15℃, a demarcation between innocuous cool and noxious cold in primates[38]. These data indicate that the behavioural response to innocuous cold in two-plate choice test is significantly impaired in PN-ZB20KO mice. Considering that both TRPA1 and TRPM8 may be involved in cold sensing, to determine

whether TRPA1 is required for in the two-plate choice test, we took advantage of the TRPA1-specific blocker HC-030031. HC-030031 could not alleviate cold-induced behavioural response of control mice (Fig. 8d). It is consistent with the results that *TRPA1*$^{-/-}$ mice were indistinguishable from control littermates when examined for behavioural responses to cold using the two-plate choice test[13]. These results suggest that TRPA1 does not mediate temperature preference. Furthermore, HC-030031 did not abolish the difference of cold sensation between control and PN-ZB20KO mice (Fig. 8d), which suggest the deficit of behavioural response of PN-ZB20KO mice to innocuous cold in two-plate choice test could not result from the deficit of TRPA1. Due to the lack of TRPM8-specific blocker[39], we could not do similar experiments to address the role of TRPM8 in temperature preference.

In the cold plate test, PN-ZB20KO and control mice were placed on a metal cold plate set at a temperature of 0℃, and their behaviour was observed. PN-ZB20KO mice displayed significantly less nocifensive behaviour (number of liftings) relative to the control mice when left on the cold plate for a 2-min period (Fig. 8e). In addition, 81.8% of control mice jumped during 2-minperiod on the cold plate, suggesting that the cold plate induces significant pain. In contrast, only 40.9% of PN-ZB20KO mice jumped (Fig. 8f). Moreover, the total number of jumps was significantly decreased in the PN-ZB20KO mice (Fig. 8g). These data indicate that the behavioural response to noxious cold is significantly impaired in PN-ZB20KO mice in the cold plate test. Furthermore, we found HC-030031 significantly alleviated cold-induced nocifensive behaviour of control mice, and abolished the difference of cold sensation between control and PN-ZB20KO mice (Fig. 8e-g). These results suggest TRPA1 is critically involved in noxious cold sensing and the defect in cold-evoked nociceptive behaviours of PN-ZB20KO mice in the cold plate test. Furthermore, we found HC-030031 significantly alleviated cold-induced nocifensive behaviour of control mice, and abolished the difference of cold sensation between control and PN-ZB20KO mice (Fig. 8e–g). These results suggest TRPA1 is critically involved in noxious cold sensing and the defect in cold-evoked nociceptive behaviours of PN-ZB20KO mice in the cold plate test.

The response to mechanical stimulation was tested by using von Frey hairs and Randall-Selitto apparatus[40]. As shown in Fig. 8h, PN-ZB20KO mice showed a statistically significant increase of paw withdraw threshold for the von Frey assay. Similarly, application of noxious pressure with Randall–Selitto apparatus revealed a pronounced analgesia in the PN-ZB20KO mice (Fig. 8i). TRPA1-specific blocker HC-030031 did not affect paw withdraw threshold to mechanical stimulus by von Frey hairs or tail pressure thresholds to noxious mechanical stimulus using Randall–Selitto test (Fig. 8h,i). These results suggest that other molecules than TRPA1 may be involved in the defect in nociception of PN-ZB20KO mice in response to mechanical stimulation.

We further investigated inflammatory pain sensation by intraplantar injection of 20μl of 5% formalin, and the time spent licking or biting the injected hindpaw in phase I (1-10 min) and phase II (10-60 min) was recorded[34]. The first phase is thought to be due to direct chemonociceptive effect of formalin, while the second one is mainly mediated by inflammatory reactions[41]. Surprisingly, PN-ZB20KO mice displayed similar nociceptive responses to 5% formalin as controls (Supplementary Fig. 10). Considering

formalin-induced pain behaviours such as licking are positively correlated with formalin concentration[42], we speculated that 5% formalin might be too high in concentration to produce the behavioural difference between control and PN-ZB20KO mice. Therefore, we used the low concentration of formalin (0.5%) for intraplantar injection as described previously[43]. As expectedly,

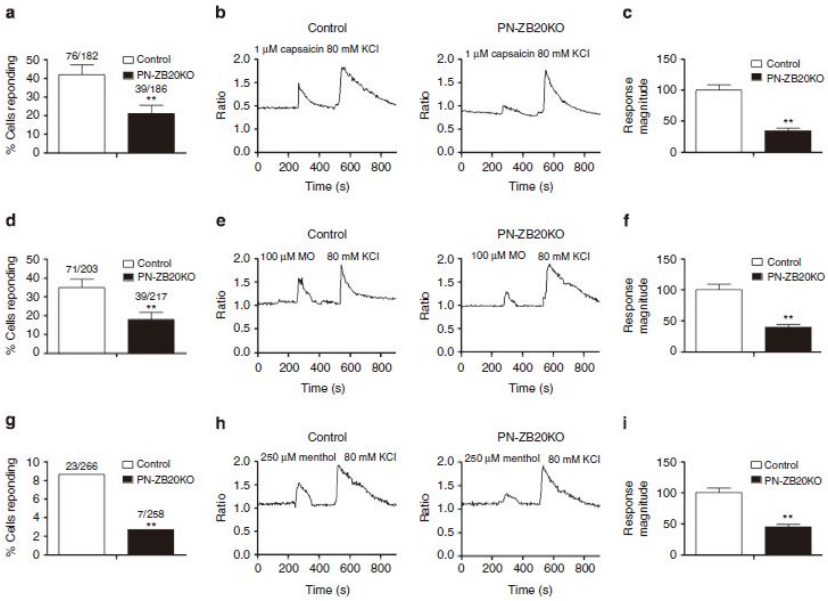

Figure 6 | TRP channels agonist-evoked calcium flux responsiveness were impaired in DRG neurons from PN-ZB20KO mice. Primary DRG neurons were isolated from adult control and PN-ZB20KO mice, stimulated with 1 μM capsaicin (TRPV1 agonist), 100 μM MO (TRPA1 agonist) or 250 μM menthol (TRPM8 agonist) and their calcium flux was monitored. **(a)** Capsaicin-responsive neurons were significantly decreased in the DRG from PNZB20KOmice. **(b)** Representative traces of $Ca2^{+}$ transients evoked by 1 μM capsaicin in DRG neurons of control and PN-ZB20KO mice. A quantity of 80mMKCl was used to check the viability of the neurons at the end of the experiment. **(c)** The response magnitude was significantly lower in the remaining capsaicin-responsive neurons from PN-ZB20KO DRG than their control counterpart. **(d)** MO-responsive neurons were significantly decreased in the DRG from PN-ZB20KO mice. **(e)** Representative traces of $Ca2^{+}$ transients evoked by 100 μM MO in DRG neurons of control and PN-ZB20KO mice. A quantity of 80mM KCl was used to check the viability of the neurons at the end of the experiment. **(f)** The response magnitude was significantly lower in the remaining MO-responsive neurons from PN-ZB20KO DRG than their control counterpart. **(g)** In neurons from PN-ZB20KO mice, the percentage of menthol-responsive neurons was significantly less than those seen in neurons from control mice. **(h)** Representative traces of Ca^{2+} transients evoked by 250 μM menthol in DRG neurons of control and PN-ZB20KO mice. A quantity of 80mM KCl was used to check the viability of the neurons at the end of the experiment. **(i)** In neurons from PN-ZB20KO mice, the magnitude of remaining responses to menthol was significantly less than those seen in neurons from control mice. The numbers of responsive and total neurons (pooled from all experiments for each genotype) are indicated in **(a,d,j). (a,c,d,f,g,i)** Data were analysed by Student's *t*-test. $^{**}P<0.01$ versus control. Values are the mean±s.e.m.

control mice showed a significant reduction in the first and second phases of the behavioural responses after injection of 20 μl of 0.5% formalin compared with those injected with 20 μl of 5% formalin (Fig. 8j,k, and Supplementary Fig. 10). Importantly, PN-ZB20KO mice displayed an impaired nociceptive response to 0.5% formalin compared with control mice

(Fig. 8j,k). It is well known that TRPA1 mediates formalin-induced nociception[43]. To further address the role of TRPA1 in the attenuated nociception of PN-ZBKO mice in response to formalin, we used HC-030031 to block TRPA1 before formalin stimulation. Intraperitoneal administration of HC-030031 preceding 0.5% formalin injection significantly decreased nociceptive responses in control and PNZB20KO mice, and more importantly, abolished the difference of 0.5% formalin-induced response between these two groups (Fig. 8j,k). These results not only support the current notion that TRPA1 is involved in formalin-evoked nociceptive behaviours[43], but also suggest that decreased TRPA1 expression in nociceptors at least partly explain the defect in formalin-induced inflammatory pain of PN-ZB20KO mice. Moreover, in another model using 20μl of 0.75% MO solution for intraplantarinjection[37], PN-ZB20KO mice also exhibited a deficit in TRPA1-mediated behavioural responses (Fig. 8l). Taken together, these data suggest that ZBTB20 in nociceptors is required for nociception and pain sensation in response to thermal, mechanical and inflammatory stimuli.

Discussion

In this study, we examined the role of ZBTB20 in the primary somatosensory system. Our findings for the first time establish ZBTB20 as a critical regulator of nociception by modulating the expression of a subset of TRP channels in nociceptors. First, ZBTB20 is specifically expressed in the vast majority of nociceptive sensory neurons in DRG. Second, disruption of ZBTB20 decreases the expression of TRPV1, TRPA1 and TRPM8 in DRG neurons, as well as their responsiveness of calcium flux and currents. Third, nociceptor-specific deletion of ZBTB20 results in a marked decrease in the pain sensitivity in response to thermal, mechanical and inflammatory stimuli.

Our findings suggest that ZBTB20 plays an essential role in the generation of fully developed nociceptors. Some transcription factors have been identified to regulate nociceptor development. Among them, Ngn1, Brna3 and Klf are critical for the formation and survival of nociceptors during their early development[20,22,23], while Runx1 is mainly involved in nociceptor diversification during their later developmental stage[18,24]. In addition, Runx1also regulates the expression of many transduction ion channels and receptors by nociceptors[18]. ZBTB20 expression is initiated in DRG neurons at E13.5, when Runx1 also starts to express. Deletion of *ZBTB20* gene either by Nestin-Cre at as early as E11 or by $Na_v1.8$-Cre at later stage (E14) does not affect the formation, survival or diversification of nociceptors, as evidenced by normal number of small DRG neurons and molecular phenotypes of peripherin, TrkA, c-Ret, CGRP and IB4 in the mutant DRG. Remarkably, nociceptor-specific deletion of ZBTB20 leads to a robust decrease in the expression of TRPV1, TRPA1 and TRPM8. As a result, the corresponding nociceptive sensory neurons, including TRPV1 neurons, TRPA1 neurons and TRPM8 high-positive neurons, are reduced in DRG by the loss of ZBTB20. In contrast to Runx1, ZBTB20 does not affect the expression of sodium channels ($Na_v1.7$, $Na_v1.8$, $Na_v1.9$), ATP-gated channel P2X3, ASIC, Mrgpr members or TRPV2 in DRG neurons. These findings suggest that ZBTB20 is a unique transcription factor regulating the terminal differentiation of a subset of nociceptors.

Our findings also suggest that ZBTB20 regulates nociception and pain sensation most likely through modulating the above TRP channels in nociceptors. PN-ZB20KO mice show

deficits in pain sensitivity evoked by thermal, mechanical and inflammatory stimulation. TRP channels have been proposed to serve as thermal sensors to temperatures ranging from noxious heat to noxious cold and thus are referred to as thermo-TRPs[4]. Among them, TRPV1 (VR1) and TRPV2 (VRL-1) respond to noxious heat, whereas TRPM8 and TRPA1 are activated by normally

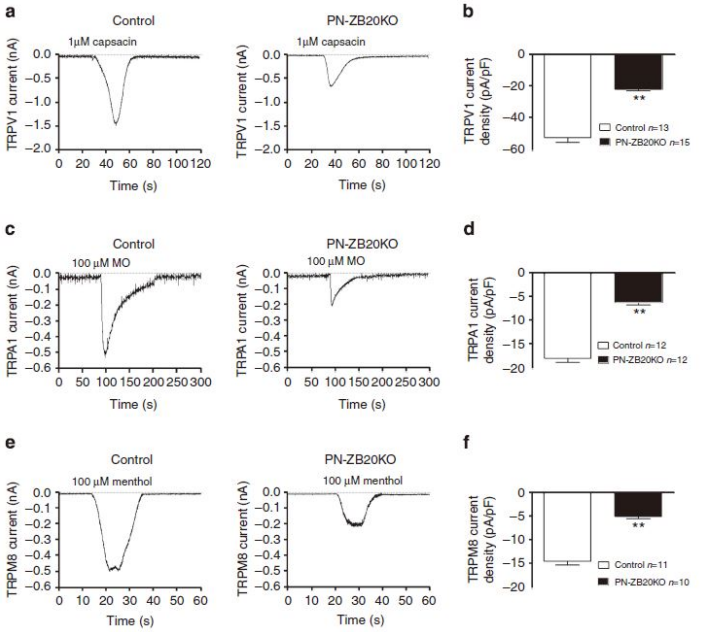

Figure 7 | Currents of TRP channels were impaired in DRG neurons from PN-ZB20KO mice. (a) Representative traces of TRPV1 current evoked by 1 μM capsaicin in DRG neurons of control and PN-ZB20KO mice. **(b)** Current density of capsaicin-activated TRPV1 current was significantly decreased in DRG neurons of PN-ZB20KO mice. **(c)** Representative traces of TRPA1 current evoked by 100 μM MO in DRG neurons of control and PN-ZB20KO mice.**(d)** Current density of MO-activated TRPA1 current was significantly decreased in DRG neurons of PN-ZB20KO mice. **(e)** Representative traces ofTRPM8 current evoked by 250 μM menthol in DRG neurons of control and PN-ZB20KO mice. **(f)** Current density of menthol-activated TRPM8 current was significantly decreased in DRG neurons of PN-ZB20KO mice. **(b,d,f)** Data were analysed by Student's *t*-test. $^{**}P<0.01$ versus control. Values are the mean±s.e.m.

innocuous cooling and noxious cold, respectively[4,11]. In the present study, we found the expressions of TRPV1, TRPM8 and TRPA1 that are known to be critical in processing pain behaviours in the DRG were decreased in the PN-ZB20KO mice.

TRPV1 serve as detectors of thermal stimuli[44,45] and mice lacking TRPV1 is impaired in thermal nociception[7]. In the tail immersion test, *TRPV1*$^{-/-}$ animals had significantly longer (three- to fourfold) mean withdrawal latencies than wild-type littermates at temperatures greater than 48℃, but normal latencies at temperatures ≤48℃. In the hot plate test, *TRPV1*$^{-/-}$ mice exhibited normal latencies at 50℃, but significantly longer response latencies than wild-type mice at temperatures greater than 50℃. PN-ZB20KO mice, in which TRPV1 is decreased by almost 50%, exhibited an intermediate phenotype consistent with their TRPV1 protein level.

Two cold-activated TRP channels have been identified in sensory neurons as transducers of cold stimulation. TRPM8 is activated at

temperatures below ~23℃ and chemicals such as menthol and icilin[10,12], while TRPA1 is activated by temperatures below 16℃ and was proposed as a sensor for painful or noxious cold stimuli[17]. Behaviourally, *TRPM8*$^{-/-}$ mice cannot discriminate between a warm and a cold surface over a wide range of temperatures that humans consider to be innocuously cool (15-30℃) or

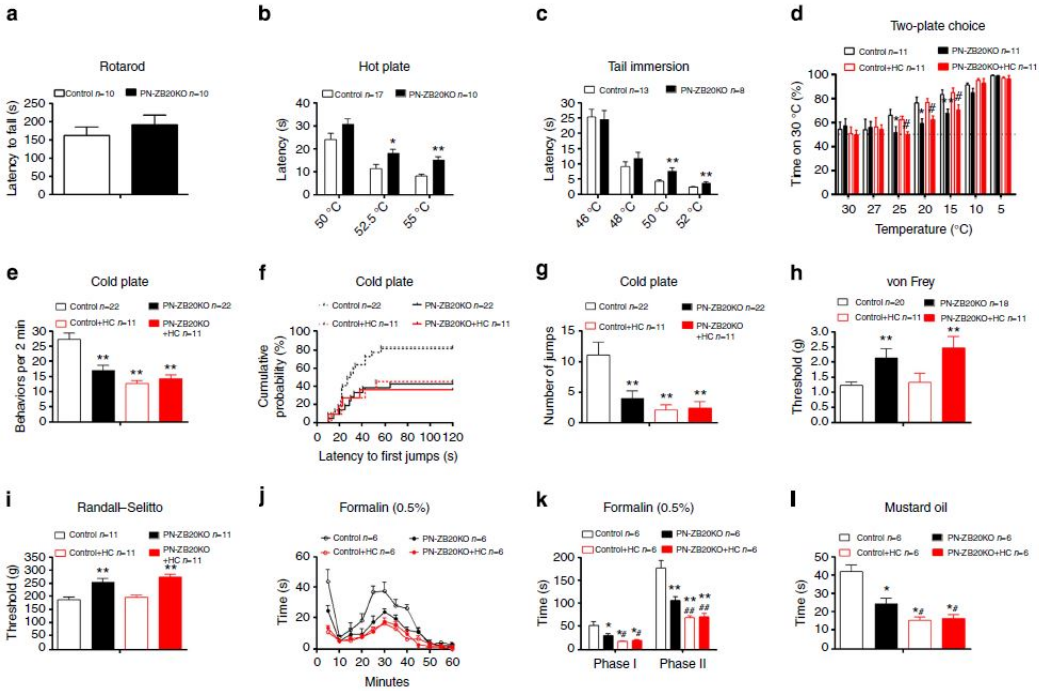

Figure 8 | Nociceptive behavioural deficits in PN-ZB20KO mice. (a) Rotarod studies showed no motor deficits in PN-ZB20KO mice. **(b)** Response latencies in the hot plate test. **(c)** Response latencies in the tail immersion test. **(d)** In the two-plate choice test, PN-ZB20KO mice showed reduced avoidance of the cooler side when the temperature is between 25 and 15℃. HC-030031 could not abolish the difference of cold sensation between control and PN-ZB20KO mice. **(e)** Cold behaviour (number of liftings) was reduced in PN-ZBKO mice in the cold plate test. **(f)** Cumulative probability plot showing the latency to the first jump off the cold plate in control and PN-ZB20KO mice. **(g)** Average number of jumps during a 2-min period on a cold plate at 0℃. HC-030031 significantly alleviated cold-induced nocifensive behaviour of control mice, and abolished the difference of cold sensation between control and PN-ZB20KO mice **(e-g)**. **(h)** PN-ZB20KO mice showed impaired behavioural response to the mechanical stimulus to the hind paw when using von Frey hairs compared with control mice. **(i)** PN-ZB20KO mice showed profound analgesia to noxious mechanical pressure when using the Randall–Selitto apparatus compared with control mice. HC-030031 did not affect paw withdraw threshold to mechanical stimulus by von Frey hairs **(h)** or withdrawal force to noxious mechanical stimulus using Randall–Selitto test **(i)**. **(j,k)** Time spent licking/biting the injected hind paw in phase I (1–10 min) and phase II (10-60 min) after intraplantar injection of 20 μl of 0.5% formalin was significantly decreased in PN-ZB20KO mice. HC-030031 significantly decreased nociceptive responses and abolished the difference of formalin-induced response between control and PN-ZB20KO mice. (l) Time spent licking/biting the injected hindpaw after intraplantar injection of 20 μl of 0.75% MO was significantly decreased in PN-ZB20KO mice. HC-030031 significantly decreased nociceptive responses and abolished the difference of MO-induced response between control and PN-ZB20KO mice. HC, HC-030031. Data were analysed by Student's *t*-test **(a–c)** or analysis of variance followed by post hoc comparisons **(d,e,g–i,k,l)**. $^{*}P<0.05$ versus control group; $^{**}P<0.01$ versus control group; $\#P<0.05$ versus PN-ZB20KO group; $\#\#P<0.01$ versus PN-ZB20KO group. Values are the mean±s.e.m.

noxiously cold (＜15℃) in the two-plate choice test[13]. In the present study, we found PN-ZB20KO mice showed reduced avoidance of the cooler side when the temperature between 25 and 15℃, which may be caused by the decreased expression and function of TRPM8 but not TRPA1, since HC-030031 could not abolish the difference of cold sensation between control and PN-ZB20KO mice. It is consistent with the results that *TRPA1*$^{-/-}$ mice were indistinguishable from control littermates when examined for behavioural responses to cold using the two-plate choice test[13], suggesting that TRPA1 does not mediate temperature preference. In the absence of well known and specific blocker of TRPM8 (ref. 39), it may not be fully verified that the deficit of temperature preference of PN-ZB20KO mice is resulted from the decreased expression and function of TRPM8, since there may be three general populations of cold-sensitive sensory neurons in DRG: those expressing TRPM8, those expressing TRPA1 and also TRPV1 and those that use neither TRPM8 nor TRPA1 for detecting cold[46].

The role of TRPA1 in noxious cold is still controversial. Some independent studies analysed the effect of TRPA1 deletion on behavioural responses to noxious cold, assessed using cold plate(0 ℃) and acetone tests. Kwan *et al.* and Karashima *et al.*[11,37] found *TRPA1*$^{-/-}$ mice showed significantly less nocifensive behaviour than control mice. Bautista *et al.*[47], however, found no difference from control. These differences may be explained by difference in methodology, different constructs for TRPA1 deletion and difficulties in assessing cold-induced pain behaviours as described by Foulkes *et al.*[48] It is worth noting that observation indexes are different in the cold plate (0˚C) test. Bautista *et al.*[47] measured paw-withdrawal latency and time to first shiver, and found responses were not significantly different. Karashima *et al.*[11] measured number of jumps, percent of mice with jump and latency to first jump and found *TRPA1*$^{-/-}$ mice showed significantly less nocifensive behaviour. Conceivably, the phenotype reflects a contribution of TRPA1 to cold sensitivity in the setting of tissue injury, but not to acute cold pain[2]. Furthermore, Karashima *et al.*[11] did not observe a significant difference in the latency to the first cold-related response such as shivering/paw rubbing, which is consistent with the result of Bautista *et al.*[47] In the present study, we compared the total number of jumps and percent of mice with jump between control and PN-ZB20KO mice. PN-ZB20KO mice displayed significantly less nocifensive behaviour of jump relative to the control mice. Since HC-030031 significantly alleviated cold-induced nocifensive behaviour of control mice, and abolished the difference of cold sensation between control and PN-ZB20KO mice, we predict that TRPA1 is involved in noxious cold sensing and the defect in cold-evoked nociceptive behaviours of PN-ZB20KO mice in the cold plate test.

The role of TRPA1 in mechanosensation is also still controversial. Bautista *et al.* and Petrus *et al.*[47,49] reported no change in mechanical thresholds in *TRPA1*$^{-/-}$ mice, whereas Kwan *et al.*[37] reported deficits. Whether and how these differential physiological effects manifest at the level of behaviour is unclear[2]. In the present study, TRPA1-specific blocker HC-030031 did not affect mechanical thresholds in control or PN-ZB20KO mice, which suggest that TRPA1 is not involved in mechanosensation in our study and the deficit in nociception of PN-ZB20KO mice in response to mechanical stimulation is not caused by the decreased expression of TRPA1. Combined with the lack of clear evidence of direct mechanical activation of the recombinant mammalian TRPA1 (ref. 50), these data raise the possibility that TRPA1 is not intrinsically mechanically sensitive. So far, the

molecular basis of mammalian mechanotransduction is far from clarified[2]. Therefore, the exact mechanisms need future study. For example, it is known that hyperpolarizing channels such as the TREK and TRAAK channels of the K2P channel family control pain produced by mechanical stimulation and both heat and cold pain perception in mice by opposing depolarization of the nociceptors[51]. The expression and function of these channels and other molecules such as $Na_v1.7$ and $Ca_v2.2$ related with mechanosensation will be investigated in the future study[2,34,52].

The formalin model is widely used for assessing inflammatory pain and evaluating the effects of analgesic compounds in laboratory animals. Formalin-induced responses in TRPM8-deficient mice at room temperature were similar to that of wild-type mice[14]. The role of TRPV1 in formalin-induced responses is controversial. Some reports show TRPV1 antagonist significantly decreased formalin- induced responses[53,54], but there are some reports indicating that formalin-induced responses in TRPV1-deficient mice were similar to that of wildtype mice[55,56]. However, at the behavioural level, pharmacologic blockade or genetic ablation of TRPA1 produced marked attenuation of the characteristic flinching, licking and lifting responses resulting from intraplantar injection of formalin[43]. These results show that TRPA1 is the principal site of formalin's pain-producing action in vivo. In the present study, PN-ZB20KO mice showed a significant reduction in 0.5% formalin-evoked pain behaviours, and intraperitoneal administration of HC-030031 preceding formalin injection significantly decreased nociceptive responses and abolished the difference of formalin-induced response between control and PN-ZB20KO mice. PN-ZB20KO mice had an intermediate phenotype compared with mice treated with HC-030031, suggesting that there may be a dosage effect in formalin-induced nociceptive responses. At low doses (≤ 0.5%), formalin interacts directly with the TRPA1 (refs. 43,57). Furthermore, after intraplantar injection of 0.5% formalin, the expression of activating transcription factor 3 (a reliable marker of nerve injury) in DRG was significantly reduced in *TRPA1*$^{-/-}$ mice, but higher doses of formalin (2% or 5%) elicited the same activating transcription factor 3 response in WT and *TRPA1*$^{-/-}$ mice[58]. These results indicate that in WT mice, high doses of formalin (＞0.5%) recruit both TRPA1- and non-TRPA1-expressing DRG neurons[58]. So, we consider it might be better to use low doses of formalin (≤ 0.5%) in the experiments of formalin-evoked pain behaviours involving TRPA1.

Channels or receptors in DRG are generally expressed in a partially overlapping or mutually exclusive fashion. In adult mice, TRPV1 and TRPM8 are distributed in different class neurons of DRG[17], and TRPA1 is largely restricted to TRPV1-positive neurons[16]. ZBTB20 protein is distributed in the majority of DRG neurons that express TRPV1, TRPA1 or TRPM8, suggesting that ZBTB20 may regulate the expression of these TRP channels in a cell-autonomous manner. It has been reported that the expression of these nociceptive ion channels is absent or significantly decreased in *Runx1*$^{-/-}$ mice[18]. In the present study, we found the expression of Runx1 mRNA was not significantly altered, so the exact mechanisms that link ZBTB20 to the expression of these channels remain unknown. In the previous studies, we have identified some direct target genes of ZBTB20, such as alpha-fetoprotein in liver[59], fructose-1,6, -bisphosphotase 1 in pancreatic β cells[60] and IκBα in macrophages[61], in which ZBTB20 function as transcriptional repressors. Logically, decrease in expression of ZBTB20 should result in increase of transcription of target genes. However, in the present study, knockout of ZBTB20 results in decreased expression of the

TRP channels. We speculate that ZBTB20 may regulate these genes by indirect mechanisms, which was supported by our ChIP results that ZBTB20 did not bind to the promoters of *TRPV1*, *TRPA1* or *TRPM8* genes.

In summary, our identification of ZBTB20 as a critical regulator for the three key TRP channels provides insight into the terminal maturation of nociceptive sensory neurons, which will help to unravel the cellular and molecular basis of nociception and pain sensation.

Acknowledgements

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Author contributions

A.-J.R., Z.X. and W.Z. designed research. A.-J.R., K.W., H.Z., A.L., X.M., Q.L., D.C. and Z.X. performed research; A.-J.R., Z.X., J.N.W., Y.-Q.D., W.-J.Y., Z.X. and W.J.Z. analysed data; and A.-J.R. and W.J.Z. wrote the paper.

Additional information

Supplementary Information accompanies this paper at http://www.nature.com/naturecommunications

重要通知

2016 年国际生理学学术大会

——生命的逻辑

中国 北京 2016 年 09 月 25-28 日

征文通知

2012 年由中国生理学会发起，联合 9 个其他国家和地区的生理学会在苏州举办的“2012 年国际生理学学术大会”获得了空前的成功，充分展示了中国生理学会的学术水平、扩大了国际影响，为我会于 2013 年在英国伯明翰获得 2021 年国际生理学联合会 (International Union of Physiological Sciences, IUPS) 在中国召开的申办权奠定了扎实的基础。2016 年是中国生理学会成立 90 周年，学会决定召开“中国生理学会 90 周年庆典暨 2016 年国际生理学学术大会”，通过庆典活动弘扬学会传统和文化，同时为在中国召开的 2021 IUPS 大会进行准备和练兵。该学术大会定于 2016 年 09 月 25 日至 28 日在北京国家会议中心举行，详情请登录会议网站：http://www.pco-online.com/icps2016/查阅。

大会组委会已经确定特邀大会报告人 7 位，分别为中国生理学会名誉会员、美国科学院院士，UCSD 的钱煦教授，英国皇家学会院士 UCL 的 Micharl Hausser 教授，日本生学会侯任主

席、Kyoto Prefectural University of Medicine 的 Yoshinori Marunaka 教授，美国科学院院士，University of Southern California 的 Larry William Swanson 教授，中国科学院院士清华大学李蓬教授、中国科学院院士，上海生命科学院张旭研究员，北京大学肖瑞平教授。

本次会议的组织形式沿用 2012 年苏州国际生理学会议的模式，即参加会议的各国家或地区学会以其学会冠名形式组织 1-3 个专题，每个专题有 4-5 个报告人，专题报告的时间是 2-2.5 小时；同时，要求其中 3 个报告人为组织该报告学会的会员，1-2 个为其他学会会员，也即每个专题报告至少要两个学会成员。报告主题由各学会根据其学会在生理学方面的研究特点确定，组织者及报告者需为相关研究领域的资深学者或有建树的青年学者。 12 个国家及地区的生理学会（美国，澳大利亚，瑞士，巴西，中国台北，日本，英国，新西兰，德国，法国，斯堪的纳维亚（丹麦、芬兰、冰岛、挪威和瑞典）及心理神经免疫学会参加会议，并组织由这些学会冠名的专题报告会合计 17 个。中国生理学会提交了冠名专题报告会 20 个。合计专题报告会 37 个，涵盖了生理学各个领域。

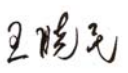
大会报告及专题报告详细情况及日程安排，请登录会议网页查看。

本次会议除大会报告和专题报告外，还设有青年工作者专场报告及墙报展示，具体要求详见征文范围。敬请各位会员踊跃投稿参会。

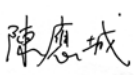
衷心感谢您对学会工作的大力支持，我们期待 9 月与各位在北京相会！

此致

敬礼！



中国生理学会理事长及大会主席　王晓民



中国生理学会副理事长及大会共同主席 陈应城

一、大会工作语言

英语

二、征文范围

生理科学各个领域及相关学科尚未正式发表的研究工作均在征集范围。

1、大会报告（Plenary lecture）：每个报告的时间为 40 分钟，讨论 5 分钟。以本人研究工作为主，并结合国际研究进展。报告人由大会学术委员会确定。

2、专题讨论会报告（Symposium）：每个报告的时间为 20 分钟，讨论 5 分钟。以本人研究工作为主，并结合国际研究进展。报告人由大会学术委员会确定。

3、青年工作者专场报告（Young physiologist presentation）： 每个报告的时间为 8 分钟，讨论 2 分钟。报告本人最近完成且尚未正式发表的研究工作。现已开始接收投稿。青年工作者是指 1975 年 1 月 1 日之后出生的青年教师，科研人员和博士后。

4、墙报展示（Poster presentation）：墙报的内容应包括标题、作者姓名和作者单位。正文简要介绍研究目的、方法、结果（要求图、表、文并茂）和结论。现已开始接受投稿。

三、征文格式要求及截至日期

大会报告及专题讨论会报告将由大会学术委员会确定，目前主要征求青年工作者专题报告和墙报展示的稿件。**投稿的具体方法和稿件格式请参看会议网页中有关投稿事宜**。投稿截止日期：**2016 年 6 月 15 日**。

四、会议注册，交费和住宿预订

1、旅费和住宿费自理。

2、会议将收取注册费（包括会议论文集出版费用和中餐费等）。

3、会议采用网上注册、交费和住宿预订，具体事宜请参看会议网页。

分类	2015 年 12 月 01 日至 2016 年 06 月 30 日	2016 年 07 月 01 日至 2016 年 08 月 31 日	2016 年 09 月 01 日至 2016 年 09 月 28 日
国内正式代表	人民币 1800 元/人	人民币 2200 元/人	人民币 2500 元/人
国内学生代表	人民币 900 元/人	人民币 1100 元/人	人民币 1300 元/人

注：学生注册时需要出示学生证，博士后须按正式代表注册。

五、会议网址

http://www.pco-online.com/icps2016/。关于大会准备工作的进程，请随时登陆查看网页的更新。

通　知

中国生理学会内分泌代谢生理专业委员会
关于召开 2016 年学术与工作会议的通知

中国生理学会内分泌代谢生理专业委员会 2016 年学术与工作会议定于 6 月 25-28 日在四川省泸州市西南医科大学召开，具体事项通知如下：

一、会议时间：

6 月 25 日报到，26-28 日开会

二、报到地点：四川省泸州市巨洋大酒店（冯志强教授安排接机、接站、接车，请直接和冯教授联系）

三、内容：

1、委员专题学术报告：

蔡德培、朱进霞、倪　鑫、桂耀庭、

马晓松、吴　珂、冯志强、蒋春雷

2、专业委员会工作会议：

（1）专业委员会工作小结

（2）主任委员、候任主任委员工作交接

（3）讨论今后活动安排及工作设想

四、费用：

委员和代表每人交会费 1000 元，学生每人 800 元，食宿自理。

按照《中国生理学会分支机构管理办法》的规定，专业委员会组织学术会议必须使用中国生理学会的发票。由于没有 POS 机，报到现场只能收取现金，并出具报销证明。如凭证明仍无法报销的，请提前将会费转至学会的帐号（**收款单位：中国生理学会；开户银行：工商行东四支行；帐号：0200 0041 0901 4480 653**）。

五、住宿（可选择）：

1. 巨洋大酒店：500 元左右/间/天（超出报销规定的建议合住）

2. 海纳宾馆：140 元左右/间/天

六、回执：

请各位委员按时出席会议，并务必于 **6 月 10 日** 前将参会名单及住宿选择报给冯志强教授，亦可通过微信“内分泌代谢专业委员会”联系。

冯教授电话：13882735828

邮箱：zhchfeng88@126.com

七、加盖中国生理学会公章的通知拟开会时发给各位，如需会前拿到通知，请与毕植宁老师联系（18502921951）。

中国生理学会

2016.4.15

中国生理学会“第十一届全国生理学教学研讨会”会议第一轮通知（会议时间推迟一周）（再次刊登）

中国生理学会原定于2016年6月24-26日在大连市召开“中国生理学会第十一届全国生理学教学研讨会”。因为“全国大学生基础医学创新实验设计大赛”的时间与我们生理学教学交流会时间完全相同，有许多教师反映他们将作为指导教师和会议组织者参加全国大学生基础医学创新实验设计大赛，经与大连医科大学协商，只好将我们生理教学会议推迟一周。

此次研讨会由中国生理学会教育工作委员会主办，大连医科大学协办。

研讨会将为全国生理学工作者提供报告生理学教学研究成果和交流教学改革经验的平台，以推动我国各类、各级院校的“生理学”课程的课程建设、教学研究和教学改革发展。会议组委会还拟邀请生理学界知名学者就生理学的教学改革的热点问题作大会专题报告，并分专题进行主题研讨。

中国生理学会欢迎各位同道踊跃向会议投寄论文摘要，通过会议组委会审查的论文摘要将在《生理通讯》增刊上刊登；会议组委会还将遴选部分投稿人在会议上发言。**不提交论文摘要的欲参会者，经会议注册并向学会缴纳注册费后亦可参加会议**。

一、会议时间和地点

时间：2016年7月1-3日（7月1日报到，2-3日会议）。

地点：大连医科大学。

二、会议主题

1. 生理学国家（省、市）重点学科和人才队伍建设的经验介绍。

2. 国家（省、市）精品资源共享课程、国家（省、市）精品视频公开课建设的经验介绍。

3. 生理学理论课教学内容和教学方法的探讨。

4. 生理学实验课教学内容和教学方法的探讨。

5. 生理学双语教学的探讨。

6. 生理学（理论课和实验课）教材建设的探讨。

7. 医学院校长学制医学专业的生理学教学探讨。

8. 综合性大学和师范院校四年制生命科学和生物技术专业的生理学教学探讨。

9. 高等中医药院校、高等职业院校和高等医药专科院校的生理学理论课和实验课教学内容、教学方法和教材建设的探讨。

10. 中等医药专科学校和中等卫生职业学校的生理学理论课和实验课教学内容、教学方法和教材建设的探讨。

11. 生理学微课、慕课等网络课程建设和教育新技术应用的经验和介绍。

12. 生理学实验室（含机能实验室）建设和改革经验介绍。

13. 生理学教学其他相关改革和经验的介绍。

三、会议论文摘要征集范围和投稿要求

1. 论文摘要征集范围：凡符合上述会议主题的论文摘要均在征集范围。

2. 论文摘要的内容：文题、作者姓名、单位、城市、邮编、通讯作者的电子邮件地址和正文，正文字数800-1000字（含标点符号）。

3. 论文摘用的编写格式：使用微软Word进行文稿编辑和排版，具体的要求为：① 页面设置为A4幅面（页边距：上下2.54 cm，左右3.17 cm），在页面左上角用黑体四号字标注以上列出的论文摘要征集范围的编号，加一空行后再输入摘要题目、作者姓名、单位、城市、邮编和摘要正文等内容；② 题目用黑体四号字居中打印；③ 作者与题目之间空一行，两位及两位上作者时，姓名之间空一字，不加标点，用楷体五号字居中打印；④ 作者单位、城市和邮编用宋体小五号字居中打印；⑤ 在正文第一行与作者单位行之间空一行，用宋体五号

字两端对齐打印，每段首行缩进二字。

4．论文摘要的投稿：请将论文摘要的电子版本用电子邮件附件方式传送至**“中国生理学会办公室，刘璐（zgslxh@126.com），肖玲（xiaoling3535@126.com）”**收，无需邮寄纸质版稿件。

5．征文截稿日期：2016 年 6 月 5 日（以电子邮件的发送日为准）。

学会将根据来稿发送会议的第二轮通知。

6．论文摘要审稿费和刊登费的收取：学会对投寄的论文摘要收取审稿费和刊登费，共计 100 元/篇。请投稿人在投寄摘要的同时，及时交纳审稿费。

投寄的稿件如果不合要求或未通过会议组委会审查的，将不被编入会议论文摘要汇编，但学会将向作者退还刊登费 70 元。

四、会议注册和注册费的标准

1．会议注册费：800 元/人（依是否为会员及注册费缴纳时间略有变化，请见下列表格）。

将用于会议所需各项会务费用、为参会者提供的会议资料和会议期间用餐等项支出。

2．注册时间和注册费的收取标准：2016 年 2 月 14 日-6 月 20 日；会议对提前注册的中国生理学会会员（交纳了第 24 届（2015 年-2018 年）会员会费者）和非会员参会者实行注册费优惠，现场注册收取全额注册费。

3．已经注册因故不能参加会议：不能退还注册费，但可换其他人参加会议。

	2016 年 4 月 30 日前注册并缴纳注册费者	2016 年 6 月 20 日前注册并缴纳注册费者	6 月 21 日以后至会议报到现场注册并缴纳注册费者
普通会员	800 元	900 元	1000 元
非会员	900 元	1000 元	1100 元
学生会员	500 元	600 元	700 元
学生非会员	600 元	700 元	800 元

4．审稿费和注册费缴纳方式（汇款时请注明：**姓名+单位+教学会议**）：

银行转账（注意不要用 ATM 机汇款，因此种汇款形式，学会得不到银行回单）：

开户单位：中国生理学会

开 户 行：工商行东四支行

银行帐号：0200004109014480653

现场注册：只接受现金（学会不具备异地刷卡的条件）

5．为提高工作效率和减少参会人员的麻烦，参会者可将会议注册费及摘要刊审费同时汇入学会账户。

五、住宿安排

会议组委会将在会议第二轮通知中告知各指定酒店的信息和联系方式，由参会者自行向各酒店预订房间。

六、招商信息

会议将组织生理学教学和科研仪器、生理学教材的展览，有意参展的厂商和出版社请与中国生理学会办公室肖玲联系（邀请函另发）。

热忱欢迎生理学教学工作者、教学管理工作者，生理学教学和科研仪器厂商代表和生理学教材出版社代表参加会议！

学会办公室联系人：肖 玲 刘璐

联系电话： 010-65278802，010-85158602

传真： 010-65278802

电子信箱： 肖玲 xiaoling3535@126.com 或 刘璐 zgslxh@126.com

中国生理学会

2016 年 2 月 14 日

中国生理学会第十一届全国生理学教学研讨会参会回执

姓 名		性别		年龄		职称或职务	
单 位							
详细联系地址						邮编	
办公电话				移动电话			
电子信箱							
交纳审刊费 √	学会帐号汇款（ ） 现场现金交纳（ ）			交纳会议注册费 √		学会帐号汇款（ ） 现场现金交纳（ ）	
备 注							

注意：征文截稿日期为 2016 年 6 月 5 日

中国生理学会新型生理学实验技术平台培训班通知（再次刊登）

提高科技人员的职业技能，加速培养高层次、复合型高素质人才是时代的迫切需要。为了更好地为实验课程开设提供科学合理的条件，促进高新技术的应用，提高实验教学师资队伍的业务素质，使之在业务和专业技能方面有长足的发展，需要有创新性的实验方法、技术和手段，并在实验教学中发挥示范和带头作用，不断提高机能学实验这门课程的教学质量。中国生理学会定于 **2016 年 7 月 25-31 日**在贵州举办“**中国生理学会新型生理学实验技术平台培训班**”。届时将聘请国内具有丰富教学与实践经验的中南大学湘雅医学院罗自强教授和山东大学医学院刘传勇教授等授课。本次学习班还将展示一些比较先进的教学仪器，学员通过上机实践操作或动物实验可掌握较多的实验新理论和技术，并就如何构建基于 Internet 的网络教学平台和国家级医学虚拟仿真实验教学中心与专家进行讨论。

授课时间：2016 年 7 月 25-31 日（7 月 24 日报到）

地点：贵州医科大学基础医学院

收费标准：1800 元/人，包括教材，实验动物，上机操作。

提前交费和报到时交费均可。汇款请注明是交纳学习班费用。

学会电汇账号：

开户单位：中国生理学会

开 户 行：工商行东四支行

银行帐号：0200004109014480653

课程内容：

专题讲座：1.罗自强教授的讲课题目是：翻转课堂的实施与思考; 2.刘传勇教授的讲课题目是：医学基础虚拟仿真实验教学的发展与展望； 3.基于信息化的下一代生物信号采集与处理系统介绍；最新 VR 技术在医学虚拟仿真实验教学中心的应用；4.药理和行为学研究设备应用技术探讨。

演示实验：1. Langendorff 心脏灌流；2.人体生理信号无线采集（血压、血氧、心电及肺活量）；3.血管环张力实验；4.大鼠无创血压测定；5.生理无线遥测实验技术；6.大鼠海马神经元放电（含大鼠脑片的制备及记录）；7.蛙类动物在体心肌细胞动作电位记录；8. VMC-100 虚拟医学院展示（虚拟医学中心软件）；9.行为学实验设备的演示（学习记忆、抑郁类）。

教学实验：1.神经干动作电位引导；2.神经干兴奋传导速度的测定；3.神经干兴奋不应期测定；4.肌肉兴奋-收缩的时相关系测定；5.蛙缝匠肌被动张力与肌梭放电同步记录；6.期前收缩-代偿间歇；7. 减压神经放电；8.大鼠心功能参数测定；9.呼吸运动调节；

10.家兔胃肠电图的记录；11.消化道平滑肌生理特性研究；12. 影响尿生成的因素；13.急性失血性休克及其挽救（配合微循环）；14.急性高血钾症；15.药物对动物血压的影响；16.药物对实验性心律失常的作用。

技能比赛：正确使用兔手术台固定动物、正确使用 BL-420N 操作系统记录家兔动脉血压。

参加学习班的学员在课程修满经考核合格后将颁发给Ⅰ类继续医学教育学分 **7** 分。欲参加学习班的老师请认真填写下列回执，并于 2016 年 7 月 15 日前发送电子版至学会电子邮箱（见下），学会将根据报名回执寄发报到通知。

欢迎从事机能实验教学与科研的老师踊跃报名。

联系人：刘璐、肖玲

电话：010－65278802　010-85158602

地址：北京东四西大街 42 号 中国生理学会　邮编：100710

电子信箱：zgslxh@126.com
lingxiao12341@sina.com

中国生理学会

2016 年 2 月 26 日

2016 年“中国生理学会新型生理学实验技术平台培训班”回执

姓名		性别		年龄		职称或职务		
单位								
联系地址							邮编	
办公电话						移动电话		
电子信箱								
备注								

注：回执请于 2016 年 7 月 15 日前发送电子版至 zgslxh@126.com　lingxiao12341@sina.com

学会活动

中国生理学会基质生物学专业委员会成立大会暨第一次全国基质生物学学术会议纪要

为促进我国基质生物学的发展，2016 年 3 月 18-20 日，“中国生理学会基质生物学专业委员会成立大会暨第一次全国基质生物学学术会议”在北京邮电会议中心成功召开，此次会议由中国生理学会基质生物学专业委员会主办，北京大学医学部承办。会议主旨一是为了庆祝中国生理学会基质生物专业委员会的正式成立，二是为我国基质生物学领域的专家学者提供一个跨领域交流与合作的平台。国际基质生物学会主席 Francesco Ramirez 教授，美国基质生物学会主席 Suneel Apte 教授，德国基质生物学会主席 Lilliana Schaefer 教授，英国血管生物学会前主席 Andrew Newby 教授以及澳大利亚与新西兰基质生物学会主席 John Whitelock 教授专程到会祝贺和参与交流，来自国内及港台 34 家单位的 150 名专家学者及青年科研人员参加了大会。

开幕式上中国生理学会基质生物学委员会主任委员孔炜教授宣布本次大会开幕，并介绍了基质生物学专业委员会成立的过程和委

员的组成。随后中国生理学会副理事长兼秘书长王韵教授致辞祝贺中国生理学会基质生物学专业委员会成立。此外，国际基质生物学会主席 Francesco Ramirez 教授发言祝贺中国生理学会基质生物学专业委员会成立，并期盼学会以后和国际及其他国家的基质生物学学会加强合作交流共同发展。

大会学术报告共分 6 个主题板块，30 名中外基质生物学专家学者分别从细胞外基质与形态发生、稳态和疾病、整合素信号转导、蛋白质水解和组织工程等多方面进行全英文学术汇报，并且与参会代表进行了充分深入的学术讨论；同时大会还设有学术壁报评比环节，17 名来自全国 12 个研究单位的青年学者就自己的在研课题进行了壁报展示，与参会专家和代表进行了深入的交流，经评委评审选出 4 名青年学者获得优秀壁报奖，分别是赵桂珍（北京大学），冯寒（北京大学）、冯国伟（南开大学）和刘畅（北京大学）。与会学者对此次会议的科学品质、跨学科特点、会议组织和会务服务都给予了很高的评价。

会议期间还召开了中国生理学会基质生物学专业委员会第一次委员大会。会上主任委员孔炜教授首先向所有委员颁发了委员证书，随后委员就学会建设及提升学科竞争力、网站改进、从纵向横向扩大学科影响力、如何增加政府资助基质领域立项、如何打造好的会议品牌等方面作了热烈讨论。委员会还初步拟定第二次全国基质生物学学术会议召开的时间。

本次大会的成功举办，促进了我国基质生物学领域跨学科的了解和交流，提供了合作的平台；并且增强了与其他国家、兄弟学会的交流，为今后深入合作奠定了基础；同时还明确了中国生理学会基质生物学专业委员会未来发展和建设的方向。

中国生理学会基质生物学专业委员会主任委员
孔炜教授致开幕词


国际基质生物学会主席、美国 Mount Sinai 医学院
Francesco Ramirez 教授作报告

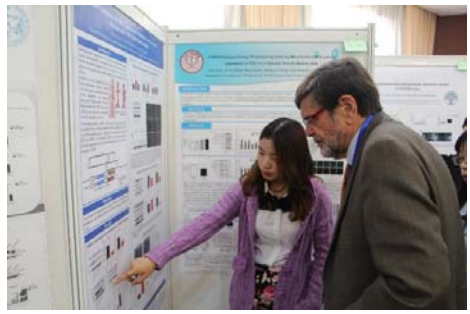

美国基质生物学会主席、美国 Cleveland 医学中心
Suneel Apte 教授作报告

德国基质生物学会主席、德国 Klinikum der Goethe 大学
Liliana Schaefer 教授作报告

英国 Bristol 心脏研究所 Andrew Newby 教授作报告

澳大利亚新南威尔士大学 John Whitelock 教授作报告

大会现场专家进行提问



壁报展示

中国生理学会基质生物学专业委员会成立大会暨第一次全国基质生物学学术会议全体参会人员合影

中国生理学会消化与营养专业委员会成立大会暨第一届学术会议胜利召开

2016 年 4 月 15-17 日，由中国生理学会消化与营养专业委员会主办的中国生理学会消化与营养专业委员会成立大会暨第一届学术会议在苏州香山国际大酒店盛大召开，来自全

国各地生理及营养专业领域的专家学者100余人参加了本次大会。中国生理学会消化与营养专业委员会主任委员、苏州大学神经科学研究所徐广银教授担任大会主席。在大会开幕式上，徐广银教授首先致开幕词，欢迎各位专家学者的到来，并给复旦大学教授杨雄里院士、中国生理学会理事长、首都医科大学副校长王晓民教授佩戴专委会会徽；随后，杨雄里院士、王晓民教授以及苏州大学副校长蒋星红教授为专委会的成立及第一届学术会议的胜利召开表示祝贺，并对在座的专注于消化与营养科学发展的学者和临床医生寄与厚望！

会议分为6个专题，分别是离子通道受体与胃肠疾病专题，脑肠轴功能可塑性专题，胃肠运动生理与功能障碍专题，胃肠粘膜与免疫专题，营养、代谢与重大疾病专题以及肝胆胰功能与疾病专题。共包含 32 个大会报告及18个墙报展示，有来自全国各地30余所高校的专家学者以口头发言或者墙报的形式展示了自己的科研成果。

在离子通道受体与胃肠疾病专题报告中，徐广银教授首先给大家介绍了离子通道受体的可塑性及其与功能性胃肠疾病的关系，以及膜片钳的基本原理和检测技术，随后介绍了课题组所取得的最新进展；来自首都医科大学的朱进霞教授作了题为“D2 和 5-HT4 受体与肠动力和血糖调节”的报告；在该专题中报告的委员还有第三军医大学董辉教授，第二军医大学马蓓教授以及苏州大学附属二院张弘弘主任。在脑肠轴功能可塑性专题报告中，上海交通大学医学院的戎伟芳教授对脑-肠轴进行了概述，脑-肠轴是一个综合的概念，它包括传入和传出神经、内分泌、营养、和中枢神经系统和胃肠道系统之间的免疫信号等；来自福建医科大学的林春教授作了题为“脊髓小胶质细在慢性内脏痛中枢敏化中的作用”的报告；山东大学医学院的刘传勇教授作了题为“硝普钠对小肠肠系膜传入神经纤维活动的作用及其机制”的报告；浙江省中医院的吕宾教授也在该专题中做了精彩报告。在胃肠运动生理与功能障碍专题报告中，武汉协和医院的侯晓华教授和上海交通大学医学院附属同仁医院王玉刚教授分别介绍了高分辨率测压在食管动力障碍疾病中的临床应用并分享了多个有趣病例。上海交通大学医学院的许文燮教授作了题为“消化道平滑肌运动单位及其意义”的报告，来自武汉协和医院的蔺蓉教授和中国医科大学的沙磊教授的报告也让现场气氛热烈，大家受益良多。在胃肠粘膜与免疫，营养、代谢与重大疾病以及肝胆胰功能与疾病等专题报告中，北京大学医学部的张炜真教授作了题为“胃肠调节糖脂代谢”的报告，中国医学科学院基础医学研究所的王林教授作了题为“生物钟在肝胆代谢中的调节和胆汁酸作为信号分子的作用机制”的报告，另外，山东大学医学院的李景新、大连医科大学附属第一医院的郭慧淑、上海长海医院的高峻、苏州大学公共卫生学院的秦立强，上海中医药大学的柯尊记、武汉协和医院的刘劲松、北京大学生命科学学院的徐成冉以及大连医科大学附属第一医院的张桂信等教授都一一作了精彩的报告，获得现场听众的热烈欢迎和一致好评！

大会于 4 月 17 日中午成功闭幕。与会专家共同讨论了消化与营养学科基础研究与临床结合等方面的研究进展及科研成果。会议期间，与会专家和学者共同合影，中国生理学会消化与营养专业委员会部分委员合影留念，大家对本届大会的成功召开给予了充分的肯定和高度的评价，并确定了下一届的学术会议将于 2017 年在武汉召开，诚挚欢迎更多的从事消化与营养专业的专家学者积极参会！

徐广银教授致辞

杨雄里院士致辞

王晓民教授致辞

蒋星红教授致辞

中国生理学会消化与营养专业委员会部分委员合影

中国生理学会消化与营养专业委员会成立大会暨第一届学术会议全体参会人员合影

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YP300 型压力换能器 测量范围：-50~300mmHg，最大耐压值：2000mmHg
YP400 型压力换能器 测量范围：-50~70mmHg，最大耐压值：300mmHg
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