［附件二　技術介紹］

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Technology/ Title	DBPR211: A Peripheral CB1 Antagonist An IND Approved First-in-Class Drug Candidate for T2DM	
Technology Type	☐Biotechnology	☐Device/Diagnostics
	■Pharmaceutical	☐Others:_____-
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Link	http://ibpr.nhri.org.tw/zhtw/wp-content/uploads/2019/02/New-2018_NCR-of-DBPR211_20181210.pdf	
Technology Description	Cannabinoid receptor 1 (CB1) is expressed in several peripheral tissues related to metabolic control in addition to its abundancy in the central nervous system. Activation of peripheral CB1 induces lipogenesis, gluconeogenesis and pancreatic β-cell death. In contrast, blockade of CB1 leads to inhibition of lipogenesis and increase of adiponectin expression, glucose uptake, and protection of β-cell survival. In-depth analysis of clinical data from Rimonabant, a centrally acting CB1 antagonist, has revealed that CB1 inhibition confined to the body's periphery has direct beneficial effects on human cardiometabolic risk factors such as insulin resistance. Besides, both clinical and preclinical studies support CB1 antagonists in treating non-alcoholic fatty liver disease (NAFLD) including non-alcoholic steatohepatitis (NASH). These data imply that targeting at peripheral CB1 is a therapeutic strategy for treating metabolic disorders such as type 2 diabetes (T2D), obesity and non-alcoholic fatty liver disease without causing the undesired psychological side effects resulting from central CB1 inhibition.	

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Intellectual Property	Patent title: Pyrazole compounds Granted USA (US 8,962,845B2); Taiwan, ROC (I472514); South Africa (ZA 201303800); Japan (特許第 5872591 號); Korea (10-1586714); China (ZL201280003742.9); Australia (2012316331); Canada (CA 2,818,944); Russia (RU 2600983); Macao (J/002325); Hong Kong (HK 1187610); India (299680); Europe (7 countries, EP263291)

	Pending PCT (PCT/US2012/056999): United Arab Emirates (application No. 567/2013); Brazil (application No. 112013013490.9)
Key Publications	1. W.C. Hsiao, K.S. Shia, Y.T. Wang, Y.N. Yeh, C.P. Chang, Y. Lin, P.H. Chen, C.H. Wu, Y.-S. Chao and M.S. Hung. A novel peripheral cannabinoid receptor 1 antagonist, BPR0912, reduces weight independently of food intake and modulates thermogenesis. ***Diabet. Obe. Metab.*** 17: 495-504, 2015. 2. C.P. Chang, C.H. Wu, J.S. Song, M.C. Chou, Y.C. Wong, Y. Lin, T.K. Yeh, A.A. Sadani, M.H. Ou, K.H. Chen, P.H. Chen, P.C. Kou, C.T. Tseng, K.H. Chang, S.L. Tseng, Y.S. Chao, M.S. Hung and K.S. Shia*. Discovery of 1-(2,4-Dichlorophenyl) -*N*-(piperidin-1-yl)-4-((pyrrolidine-1-sulfonamido)methyl)-5-(5-((4 -(trifluoromethyl) phenyl)ethynyl) thiophen-2-yl)-*1H*-pyrazole-3-carboxamide as a Novel Peripherally Restricted Cannabinoid-1 Receptor Antagonist with Significant Weight-Loss Efficacy in DIO Mice. ***J. Med. Chem.*** 56: 9920-9933, 2013. 3. R.S. Vijayakumar, Y. Lin, K.S. Shia, Y.N. Yeh, W.P. Hsieh, W.C. Hsiao, C.P. Chang, Y.S. Chao, and M.S. Hung. Induction of fatty acid oxidation resists weight gain, ameliorates hepatic steatosis, and reduces cardiometabolic risk factors. ***Int. J. Obesity*** 36: 999-1006, 2012. 4. M.S. Hung, C.P. Chang, T.C. Li, T.K. Yeh, J.S. Song, Y. Lin, C.H. Wu, P.C. Kuo, P. K. Amancha, Y.C. Wong, W.C. Hsiao, Y.S. Chao, K.S. Shia. Discovery of 1-(2,4-Dichlorophenyl)-4-ethyl-5-(5-(2-(4-trifluoromethyl)phenyl) ethynyl) thiophen-2-yl)-*N*-(piperidin-1-yl)-1*H*-pyrazole-3-carboxamide as a potential peripheral cannabinoid-1 receptor inverse agonist. ***ChemMedChem***. 5: 1439-1443, 2010.
Business Opportunity	The global population of patients with diabetes caused by excessive obesity and the improvement of the quality of life is growing rapidly, leading to an expanding market demand. Currently, only few T2D drugs show a favorable effect on weight control. Our invention exhibits potential beneficial effects on improving metabolic disorders, and thus provides an alternative for the treatment of T2D with

	additional benefits in weight loss and amelioration of NAFLD. This unique mechanism may potentially render DBPR211 as a highly competitive first-in-class drug candidate for T2D, obesity and NAFLD/NASH.