

2017 Taiwan Biotechnology Delegation

October 30 ~ November 7, 2017

Novel Therapeutic Targets and Biomarkers for Autoimmune Diseases, Type 2 Diabetes, and Cancers

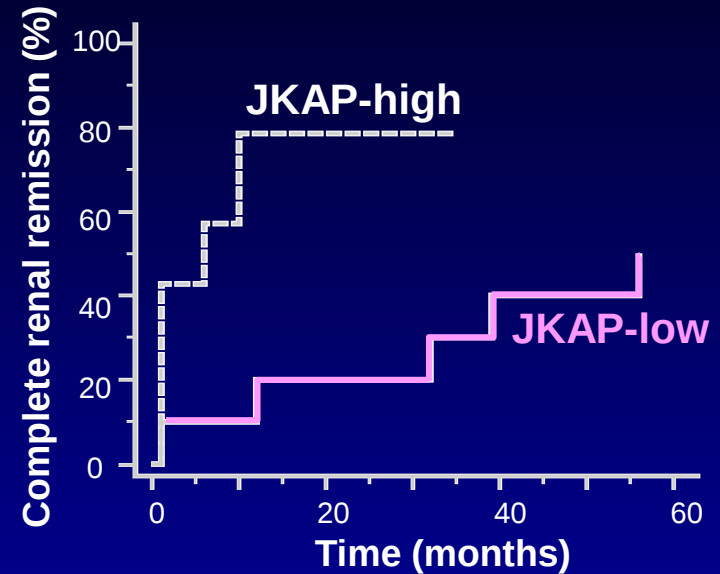
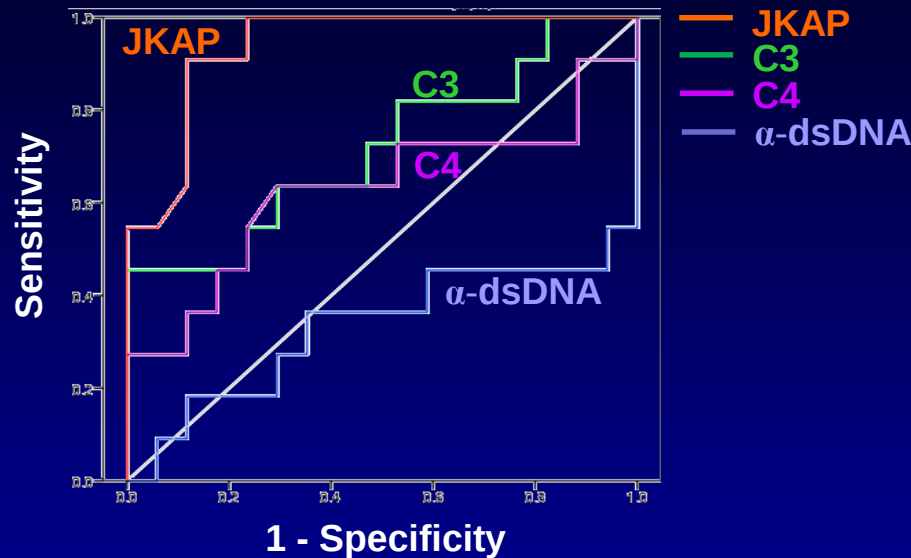


Tse-Hua Tan, PhD
Distinguished Investigator / Director
Immunology Research Center
National Health Research Institutes, Taiwan

Novel Medical Application for Human Disease

Biomarker / Target	Medical Application
DUSP22 (JKAP) ↓	Non-invasive diagnostic kit and agonist: Lupus nephritis
MAP4K1 (HPK1) ↓	Inhibitor : Immune boost adjuvant for anti-tumor immunity or vaccination
MAP4K4 (HGK) ↓	Diagnosis kit and agonist : Non-obese type 2 diabetes
MAP4K3 (GLK) ↑	Diagnostic kit and Inhibitor: Multiple autoimmune diseases and cancers

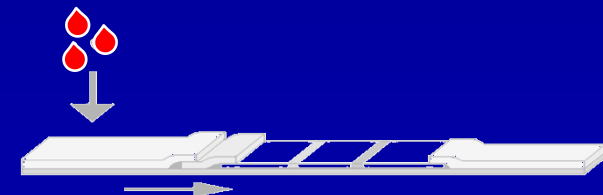
DUSP22 (JKAP) Downregulation in T Cells : Diagnostic and Prognostic Biomarker for Systemic Lupus Erythematosus (SLE) Nephritis



- DUSP22 (JKAP) downregulation in T cells correlates with nephritis and poor renal outcome in SLE
- 60% SLE patients have lupus nephritis, which is diagnosed by invasive renal biopsy

~~Invasive
renal biopsy~~

➔ Novel diagnostic kit for
lupus nephritis



MAP4K1 (HPK1) Downregulation in T Cells : Enhancement of T-cell Mediated Immune Responses

- MAP4K1 (HPK1) downregulation in peripheral blood cells and T cells from psoriatic arthritis and systemic lupus erythematosus (SLE) patients, respectively
- MAP4K1 (HPK1) is a **negative regulator** of T-cell activation

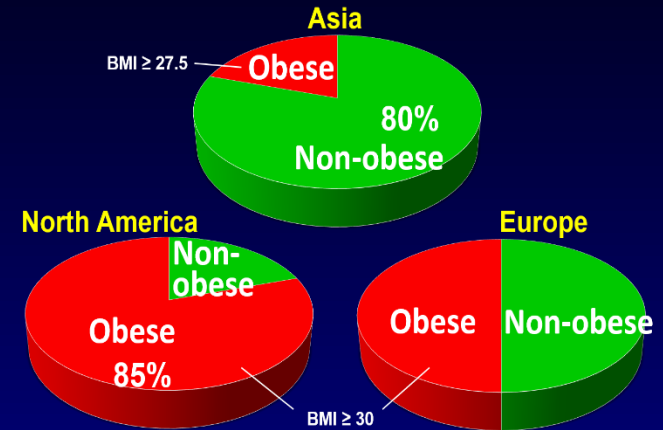
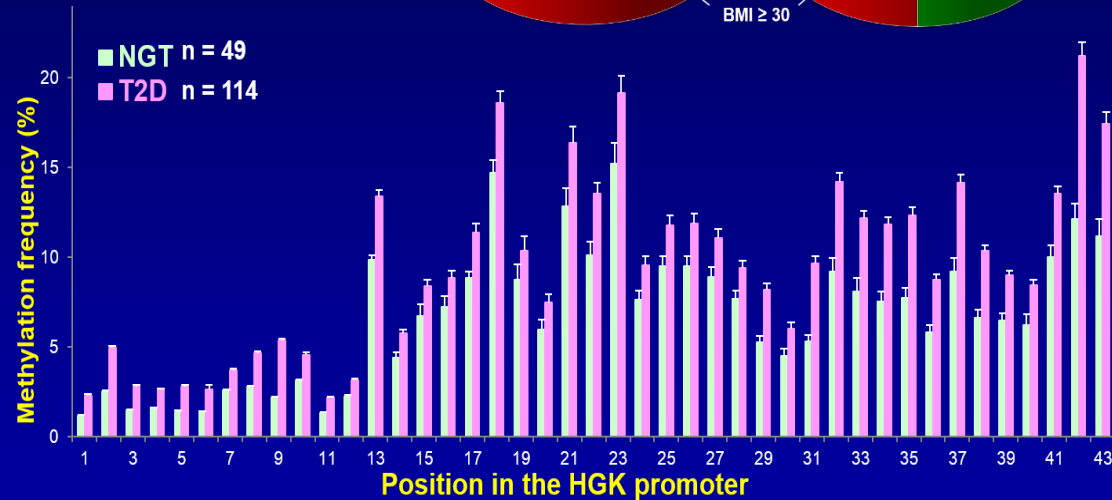
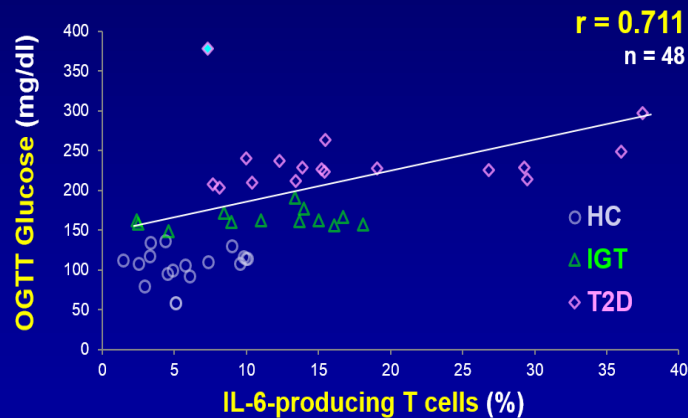
Nature Immunology 8:84, 2007

J. Biol. Chem. 287:34091, 2012

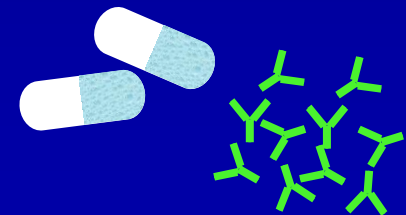
➔ **HPK1 inhibitor is a cancer immunotherapeutic drug or vaccine adjuvant**

MAP4K4 (HGK) Downregulation in T Cells : Diagnostic Biomarker and Therapeutic Target for Non-obese Type 2 Diabetes

- Non-obese T2D comprises about 80% of T2D cases in Asia
- MAP4K4 (HGK) methylation frequencies are correlated with OGTT glucose levels in non-obese T2D patients



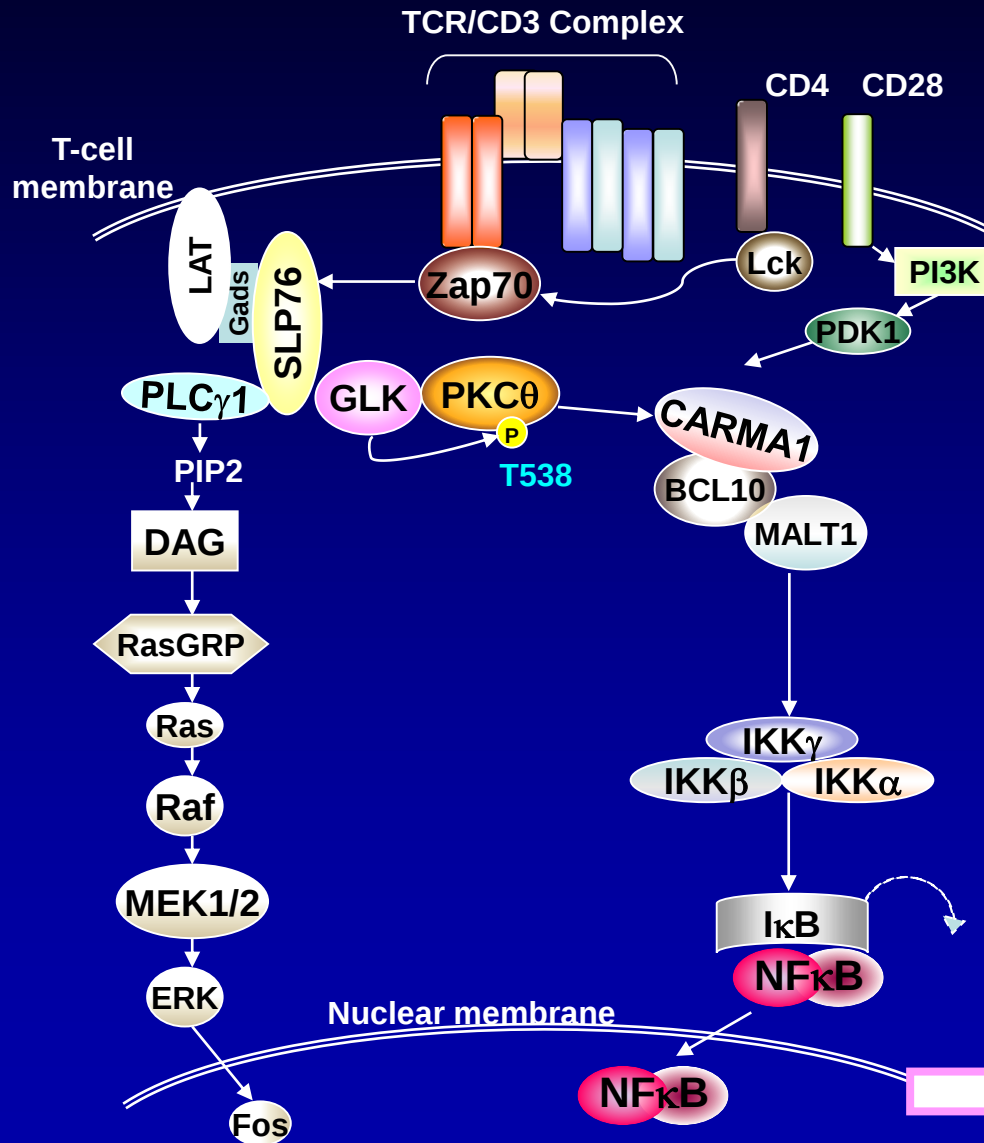
➔ Novel diagnostic kit or therapeutic drug for T2D



Diseases Showing MAP4K3 (GLK) Overexpression

Autoimmune Disease	Cancer
Systemic lupus erythematosus (SLE)	Non-small-cell lung carcinoma (NSCLC)
Rheumatoid arthritis (RA)	Hepatoma
Adult onset Still's disease (AOSD)	Glioblastoma
Graves' disease (GD)	Pancreatic ductal adenocarcinoma (PDA)
Sjogren's syndrome (SS)	Breast cancer
Ankylosing spondylitis (AS)	Esophageal carcinoma
Neuromyelitis optica (NMO)	
Alopecia	

MAP4K3 (GLK) as a Biomarker and Therapeutic Target for Autoimmune Disease, Cancer, Inflammation and IL-17-associated Disease



Nature Immunology, 2011

BMC Medicine, 2012

Arthritis & Rheumatism, 2013

Oncotarget, 2016 May

Oncotarget, 2016 June

US Patent, 2014

European Patent, 2017

Korea Patent, 2016

Taiwan Patent, 2015

China Patent, 2017

**Autoimmune diseases
(SLE, RA, AOSD)**

**Cancers
(lung, liver)**

IL-17A,

Cytokines