Novel and emerging therapies for patients with Diabetes and CKD

A/Prof Robyn Langham
St. Vincent's Hospital
Fitzroy, Australia

Disclosures

- Past consultant for Fibrotech Therapeutics
- Speaker fees; Amgen, Shire, Janssen-Cilag
- Advisory Board; Janssen-Cilag, Orphan, MSD, GSK, Amgen.

Editorial

Linking Metabolism and Immunology: Diabetic Nephropathy Is an Inflammatory Disease

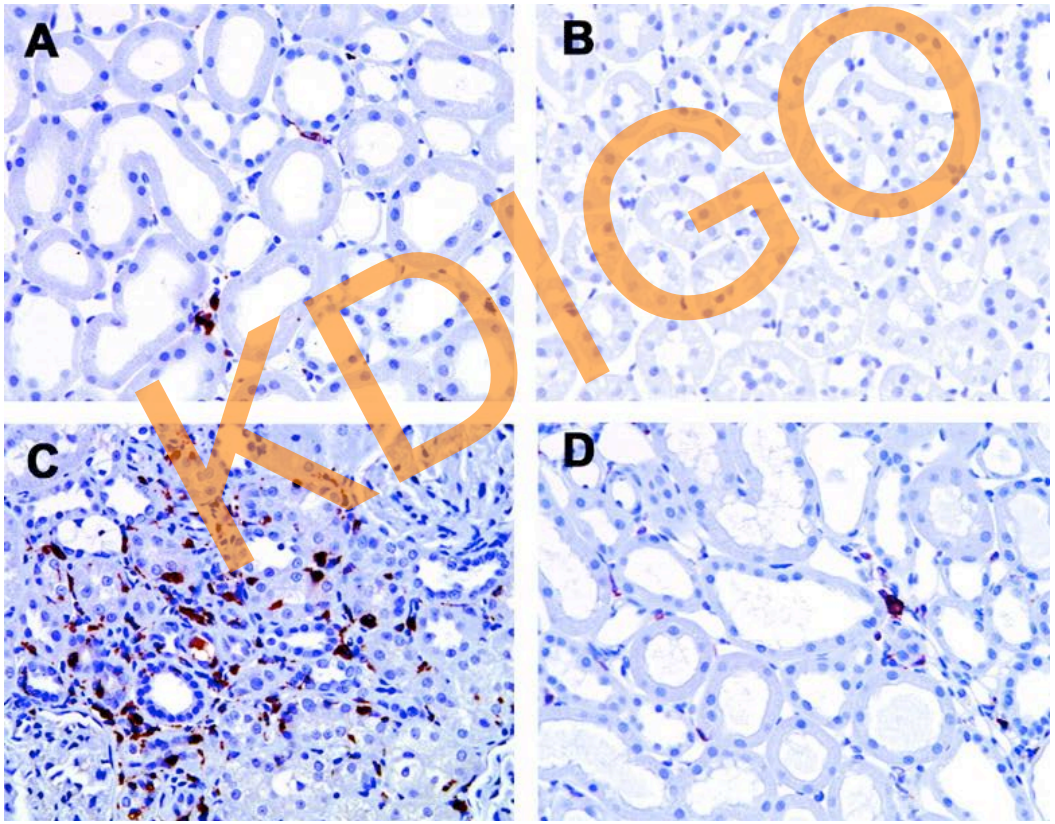
Katherine R. Tuttle

Providence Medical Research Center, The Heart Institute and Sacred Heart Medical Center, Spokane, Washington

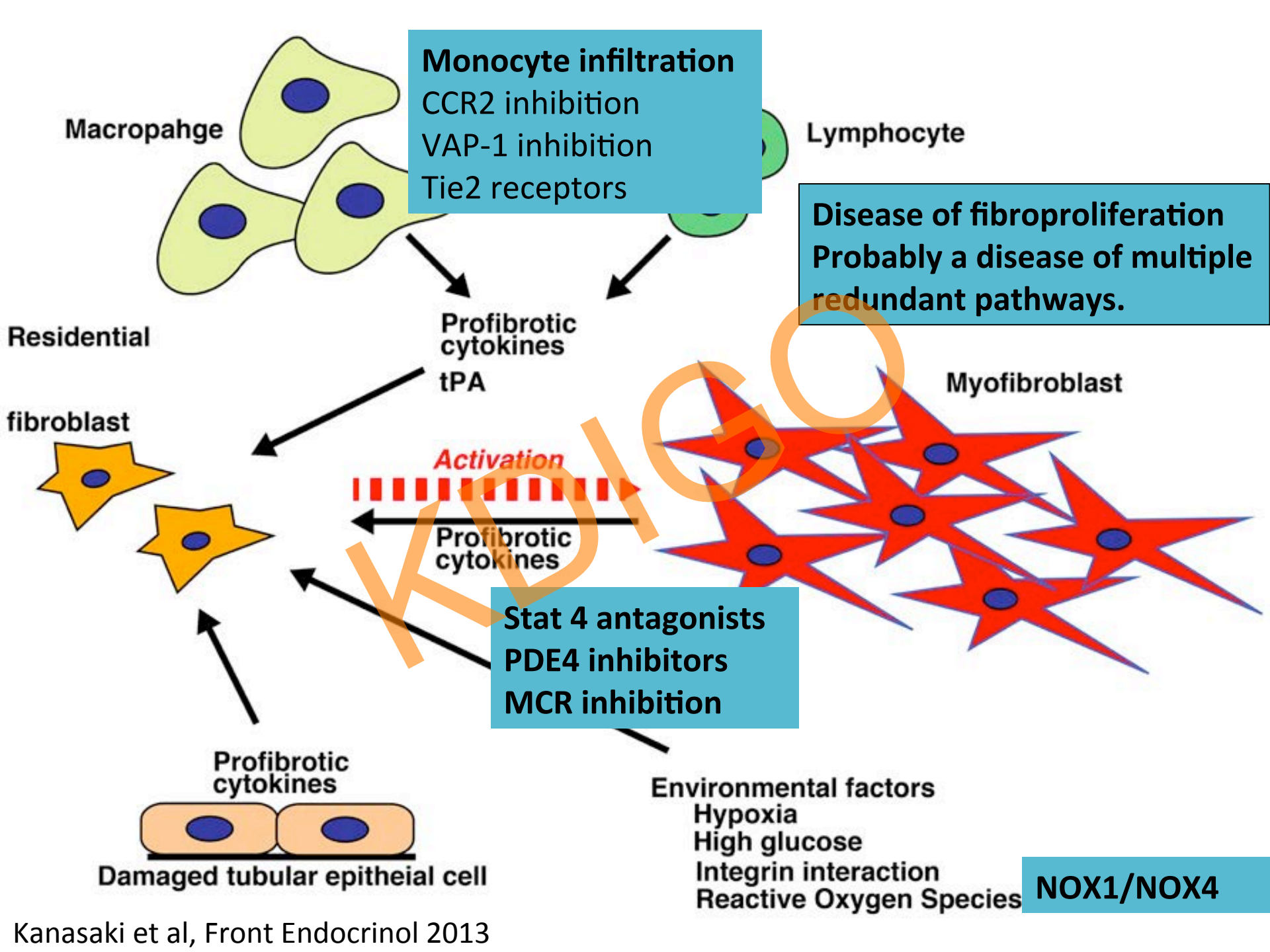
J Am Soc Nephrol 16: 1537–1538, 2005. doi: 10.1681/ASN.2005040393

"… diabetic nephropathy can be viewed as an inflammatory disease triggered by disordered metabolism."

Protein Kinase Cβ Inhibition Attenuates Osteopontin Expression, Macrophage Recruitment, and Tubulointerstitial Injury in Advanced Experimental Diabetic Nephropathy



Kelly et al., JASN 2005



Kanasaki et al, Front Endocrinol 2013

Reactive Oxygen Species – NOX inhibitors

PNAS 2000

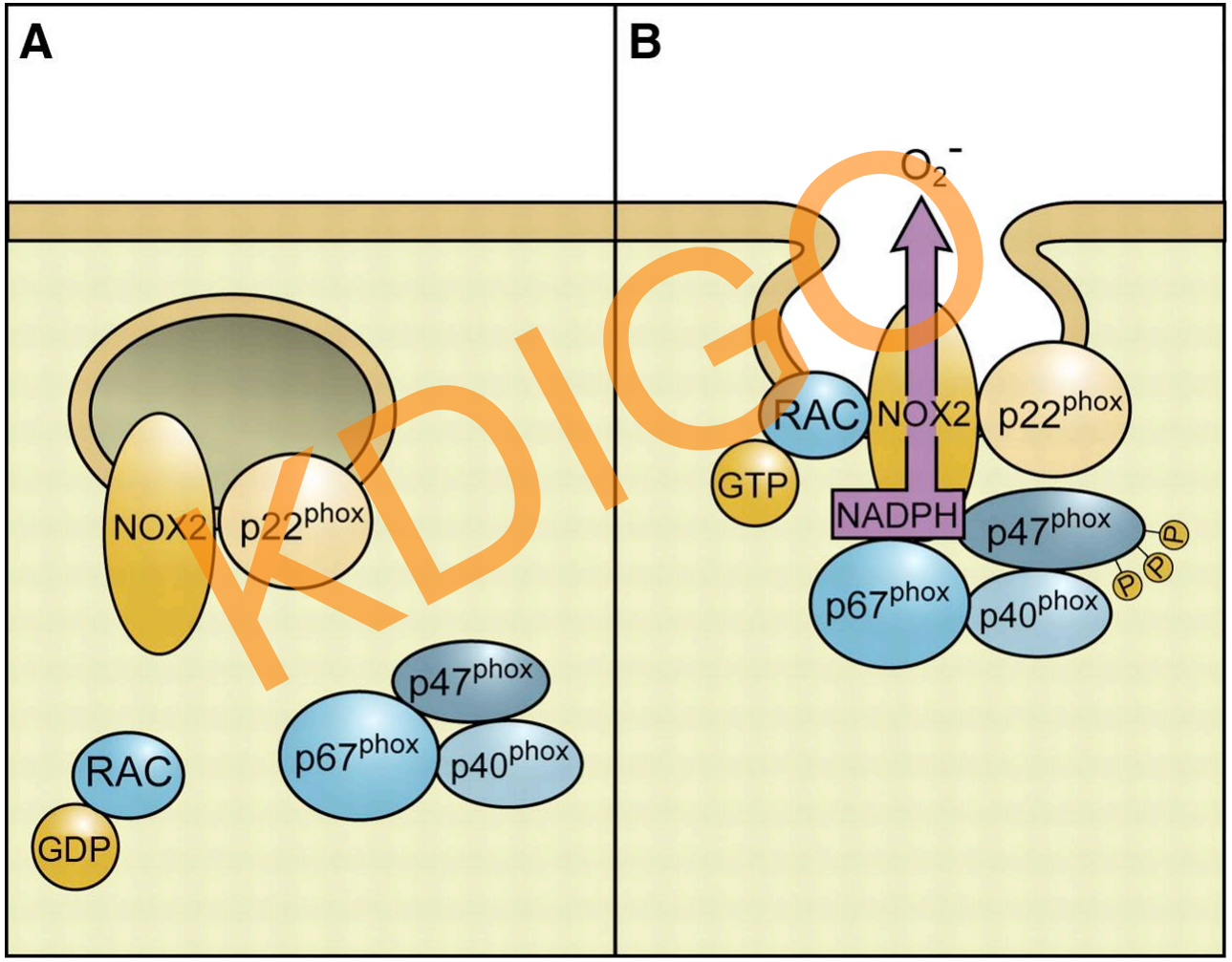
Identification of Renox, an NAD(P)H oxidase in kidney

Miklós Geiszt*, Jeffrey B. Kopp†, Péter Várnai‡, and Thomas L. Leto*§

*Laboratory of Host Defenses, National Institute of Allergy and Infectious Diseases, †Kidney Disease Section, National Institute of Diabetes and Digestive and Kidney Diseases, and ‡Endocrinology and Reproduction Branch, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD 20892

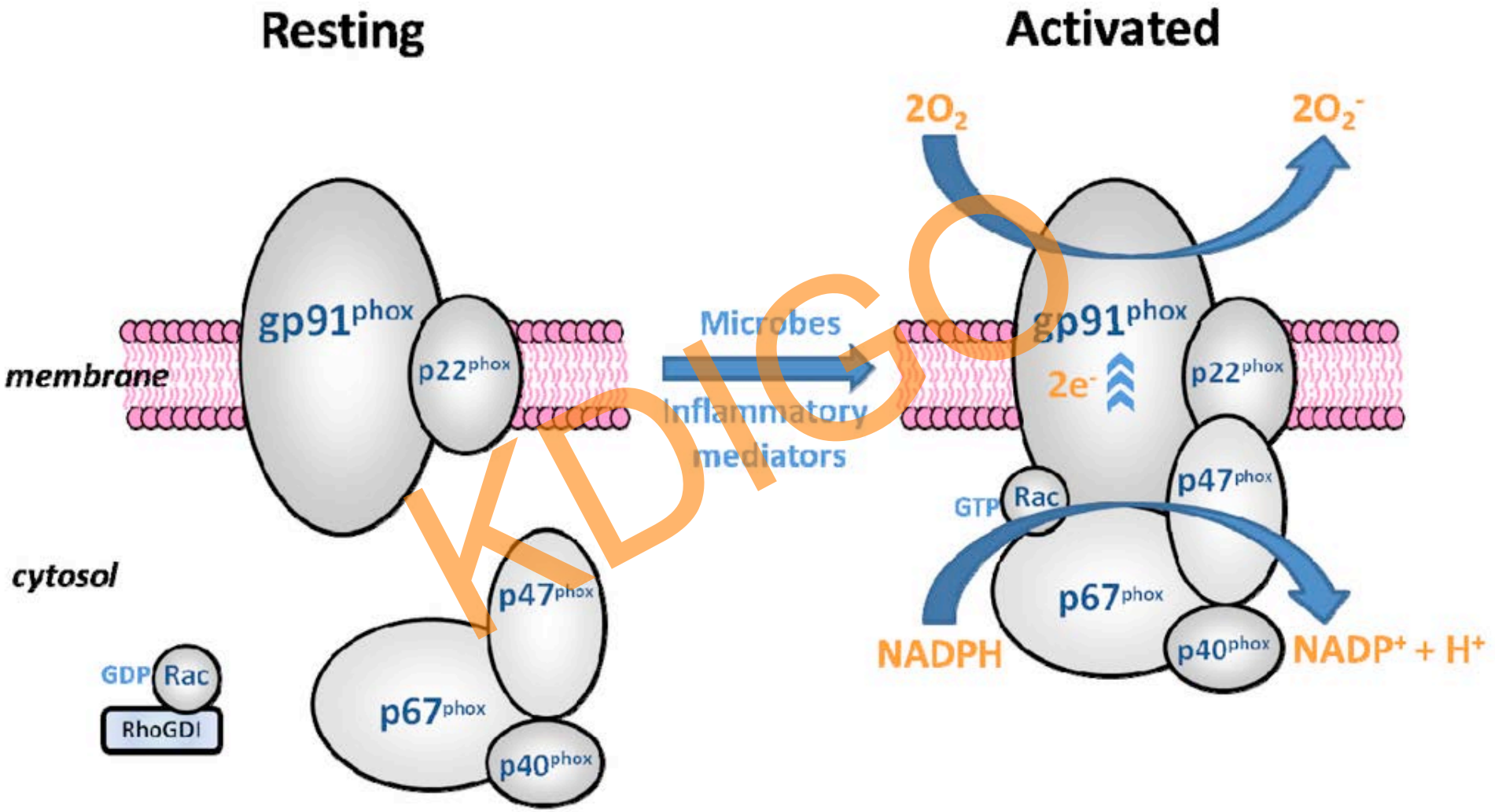
Edited by Irwin Fridovich, Duke University Medical Center, Durham, NC, and approved May 3, 2000 (received for review March 27, 2000)

NAPDH Oxidases – phagocytosis of microbes

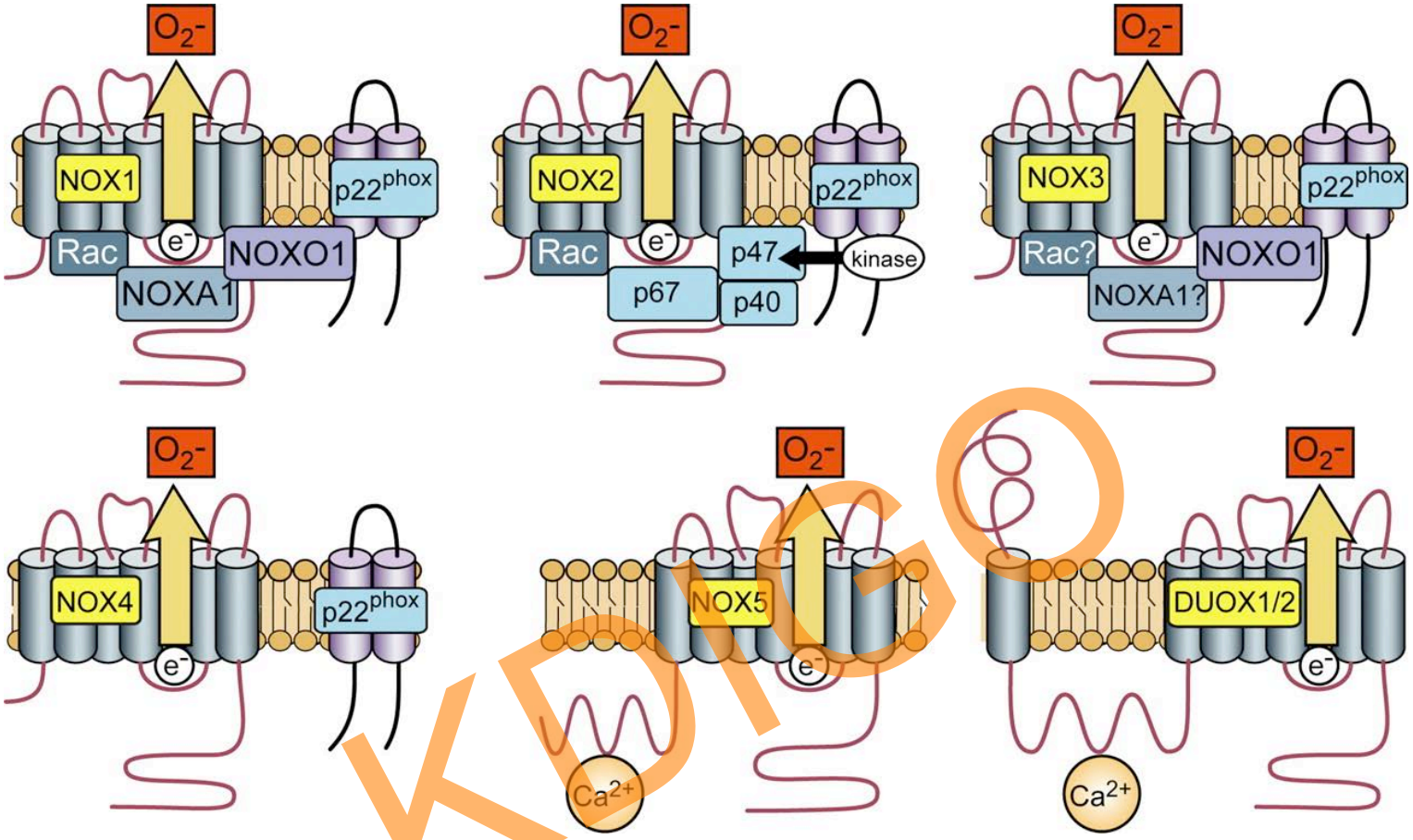


The NOX Family of ROS-Generating NADPH Oxidases: Physiology and Pathophysiology
Bedard and Krause Physiological Reviews 2007

NAPDH Oxidases – non-phagocytic



McCann and Roulston, *Brain Sci.* **2013**

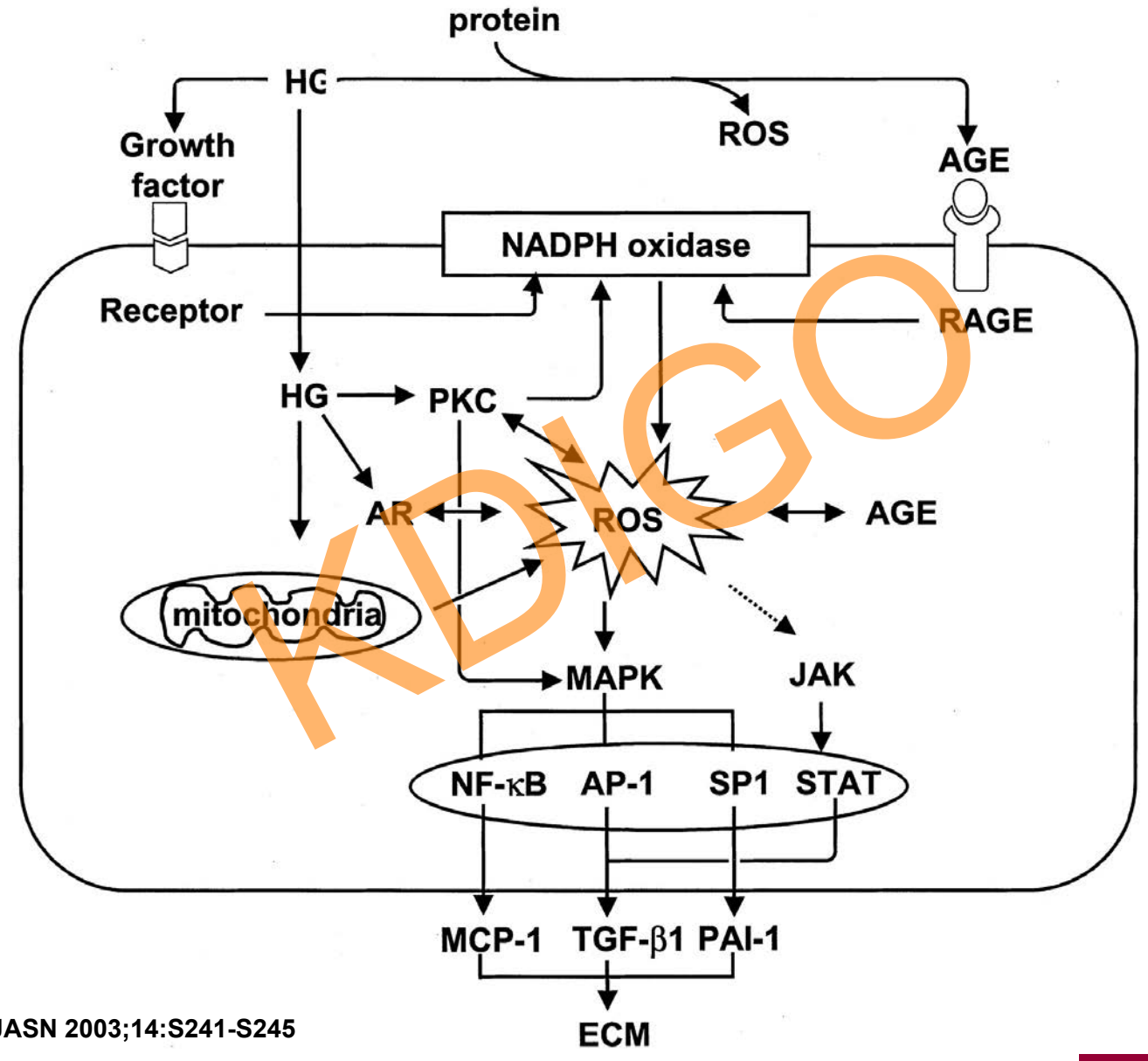


In kidney Nox 4 is the most important, ROS is important in regulation of cell cycle, also involved in renal haemodynamics and renal ion transport

NOX 4 may be mechanosensitive
- excess of ROS - = disease.

Bedard and Krause Physiological Reviews 2007

ROS-Regulated Signaling Pathways in Diabetic Nephropathy



Lee H B et al. JASN 2003;14:S241-S245

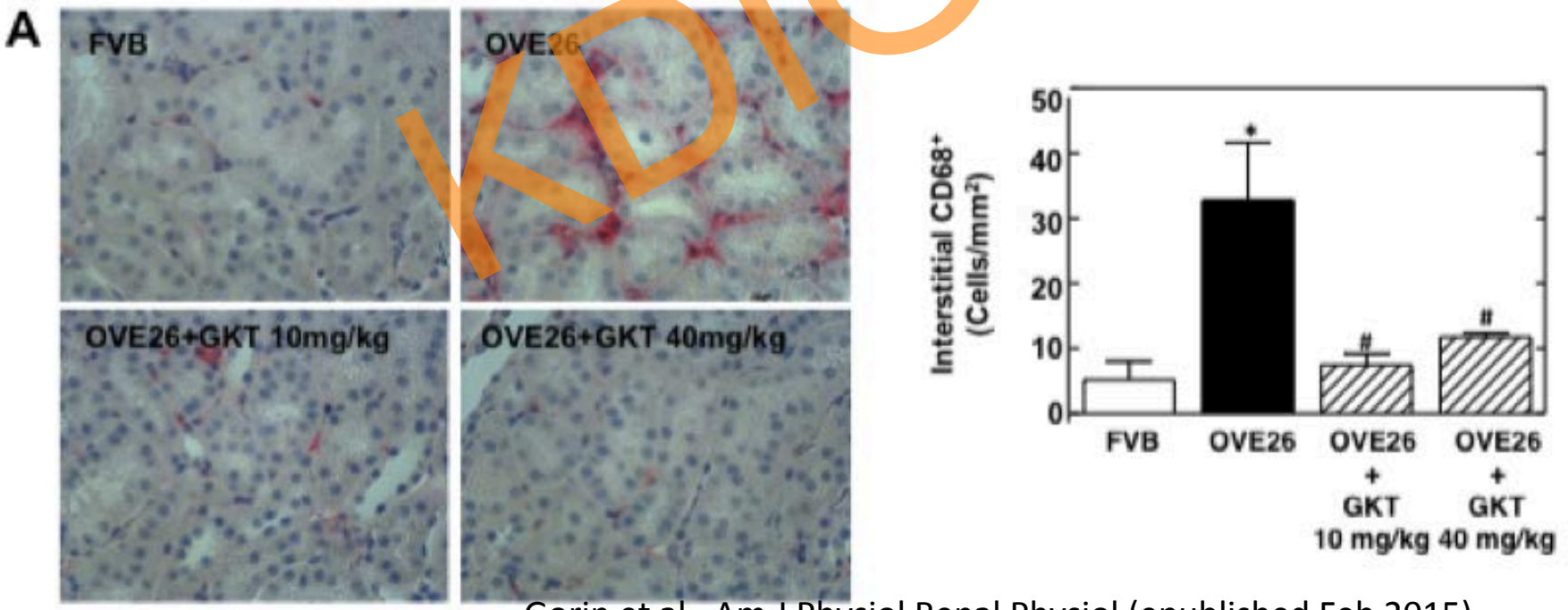
BASIC RESEARCH www.jasn.org

J Am Soc Nephrol. 2010

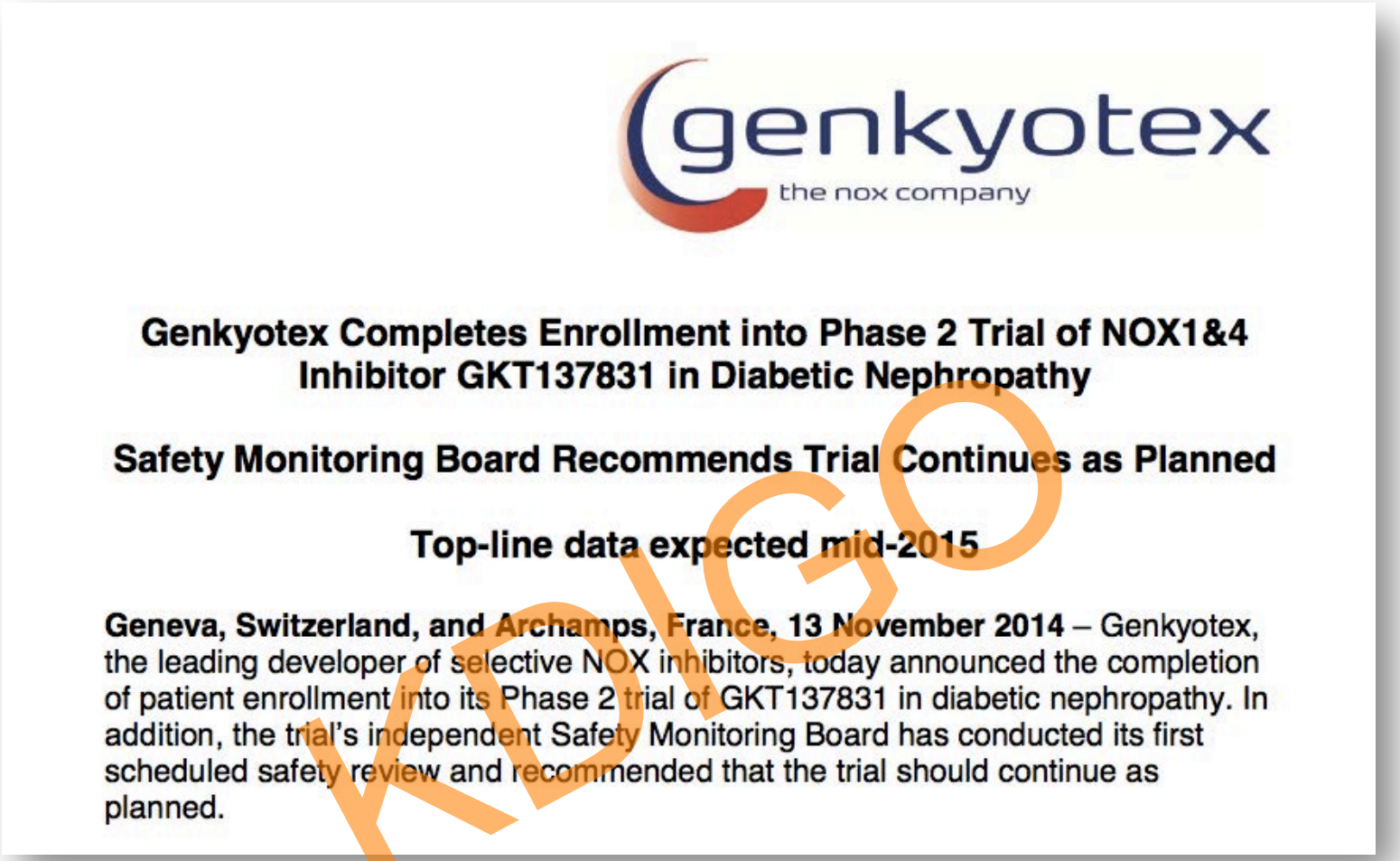
NAD(P)H Oxidase Mediates TGF-β1–Induced

BASIC RESEARCH www.jasn.org JASN June 2014 vol. 25 no. 6 1237-1254

Genetic Targeting or Pharmacologic Inhibition of



Gorin et al., Am J Physiol Renal Physiol (epublished Feb 2015)


genkyotex
the nox company

Genkyotex Completes Enrollment into Phase 2 Trial of NOX1&4 Inhibitor GKT137831 in Diabetic Nephropathy

Safety Monitoring Board Recommends Trial Continues as Planned

Top-line data expected mid-2015

Geneva, Switzerland, and Archamps, France, 13 November 2014 – Genkyotex, the leading developer of selective NOX inhibitors, today announced the completion of patient enrollment into its Phase 2 trial of GKT137831 in diabetic nephropathy. In addition, the trial's independent Safety Monitoring Board has conducted its first scheduled safety review and recommended that the trial should continue as planned.

Safety and Efficacy of Oral GKT137831 in Patient With Type 2 Diabetes and Albuminuria
NCT02010242
12 weeks, bd dose of **GKT137831, 100mg bd and 200mg bd,**
Endpoints UACR, delta UACR, secondary endpoints erectile dysfunction and neuropathic pain.

www.genkyotex.com

American Journal of Respiratory Cell and Molecular Biology, 2012

HEPATOLOGY
Official Journal of the American Association for the Study of Liver Diseases

Hepatology 2012

Nicotinamide Adenine Dinucleotide Phosphate Oxidase in Experimental Liver Fibrosis: GKT137831 as a Novel

Circulation – online Jan 2015

NADPH Oxidase 4 Induces Cardiac Fibrosis and Hypertrophy Through Activating Akt/mTOR and NFκB Signaling Pathways

Running title: *Zhao et al.; Nox4-Associated Signaling Pathways in Cardiac Remodeling*

Qingwei David Zhao, MD, PhD; Suryavathi Viswanadhapalli, PhD; Paul Williams, BS;

Qian Shi, PhD; Chunyan Tan, MD; Xiaolan Yi, MD, PhD; Basant Bhandari, PhD;

Hanna E. Abboud, MD

MicroRNA-21 – a potential anti-fibrotic

BASIC RESEARCH www.jasn.org

Lai et al., JASN 2014

MicroRNA-21 in Glomerular Injury

Jennifer Y. Lai,* Jinghui Luo,*† Christopher O'Connor,* Xiaohong Jing,‡ Viji Nair,* Wenjun Ju,* Ann Randolph,* Iddo Z. Ben-Dov,§ Regina N. Matar,* Daniel Briskin,§ Jiri Zavadil,‖ Robert G. Nelson,¶ Thomas Tuschl,§ Frank C. Brosius III,* Matthias Kretzler,* and Markus Bitzer*‡

*Internal Medicine, University of Michigan, Ann Arbor, Michigan; †Department of Pharmaceutical Sciences, Nanfang Hospital, Southern Medical University, Guangzhou, China; ‡Department of Medicine, Albert Einstein College of Medicine, Bronx, New York; §Howard Hughes Medical Institute, The Rockefeller University, New York, New York; ‖Department of Pathology and NYU Center for Health Informatics and Bioinformatics, New York University School of Medicine, New York; and ¶National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Phoenix, Arizona USA

[4]Division of Transplantation, Lahey Clinic Medical Center, Burlington

[5]Tufts University, Boston, Massachusetts, USA

[6]Division of Nephrology, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA

Monocyte infiltration – CCL2

CCL2 (MCP-1)

Recruits monocytes, memory T-cells and dendritic cells to sites of inflammation produced either by tissue injury or infection.

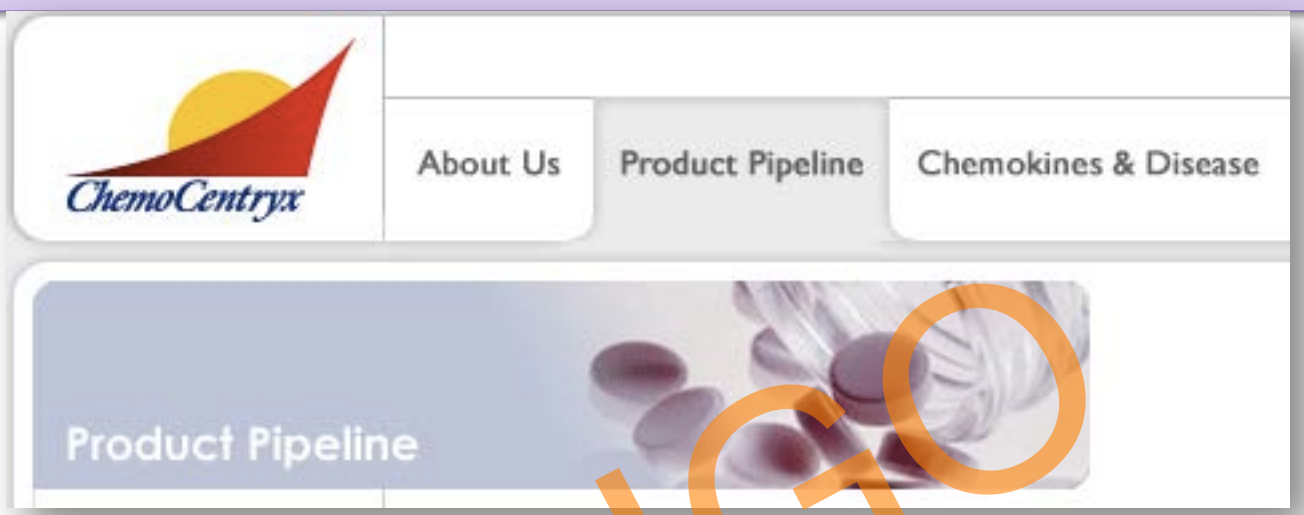
Receptors – CCR2 and CCR4 (G-protein coupled receptors)

?Role of hypomethylation of CpG sites within the CCL2 promoter region in increased CCL2 levels in serum of patients with diabetes.

Well-described role in experimental renal fibrosis, also is involved in the inflammatory milleau of diseases of neurodegeneration

Bindarit (Phase 2a) reduction in CCL2 production (NCT01109212)

CCR2 antagonist



CCX-140, completed and reported phase 2

- 52 week data from Ph II clinical trial – oral
- 332 patients, placebo, 5mg, 10mg.
- 5mg daily, reduction in UACR ($p<0.0148$)
- Attenuated annual decline eGFR (1.3 vs 2.3)
- NCT01440257
- http://www.chemocentryx.com/product/CCR2.html

CCR2 antagonist

Emapticap pegol (NOX-E36)

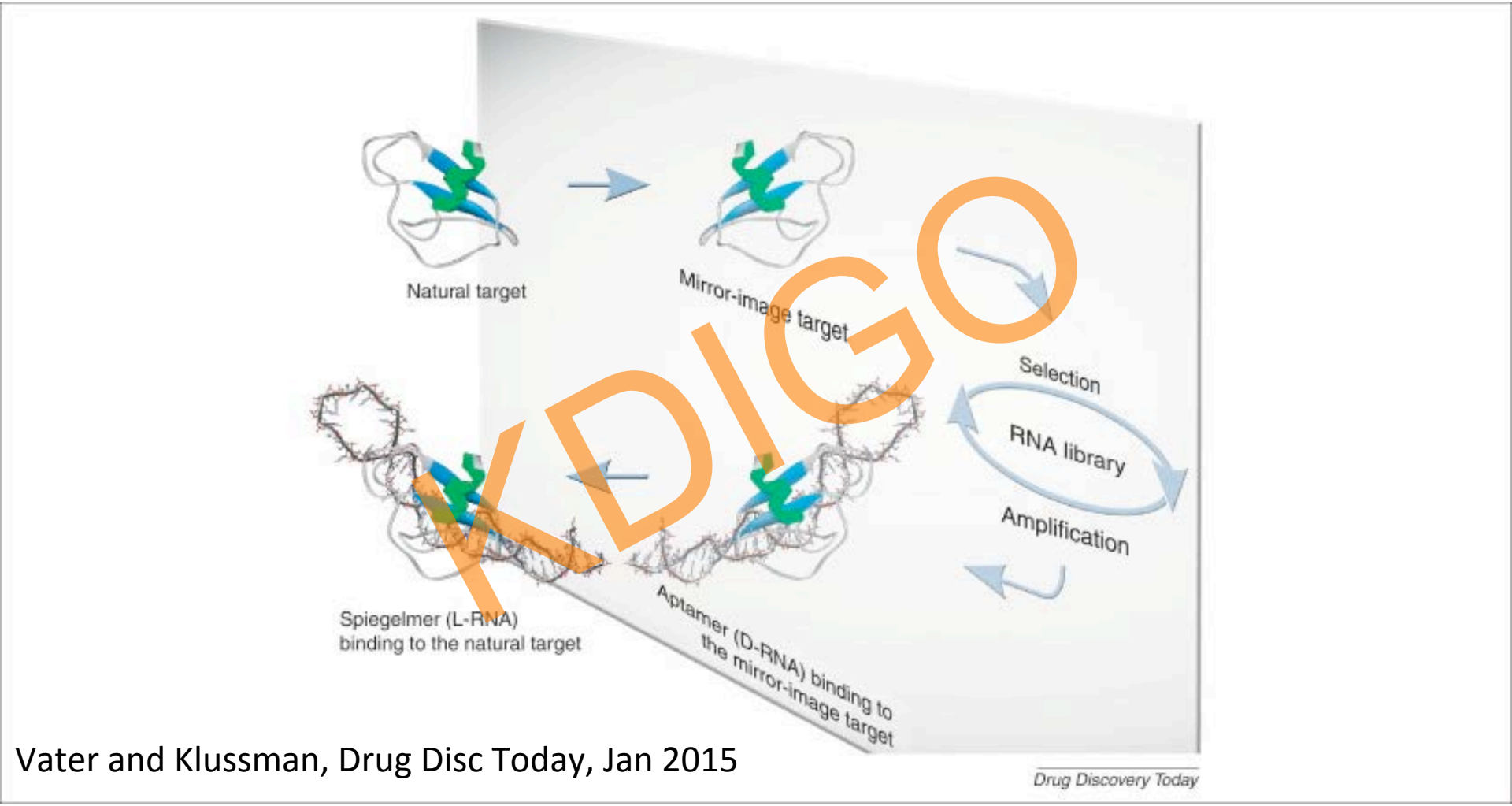
NOXXON Pharma

Phase 2A, presented ERA/EDTA 2014

RCT phase 2a, 72 patients with Type 2 diabetes and albuminuria

SC administration, twice a week, reduction in ACR (32% lower at 12 weeks), 50% reduction 31% v6%)

Benefits on glucose control



Vater and Klussman, Drug Disc Today, Jan 2015

Spieglemer – RNA, DNA based aptemers, 3D structure, stabilised against cleavage by naturally occurring endo and exonucleases. ..

Proximagen

http://proximagen.com/

Novel GPCR ?type

-has other CCR2 antagonist for neurodegen disease

Cytokine & Growth Factor Reviews 24 (2013) 23–40

Contents lists available at SciVerse ScienceDirect

Cytokine & Growth Factor Reviews

journal homepage: www.elsevier.com/locate/cytogfr

ELSEVIER

Survey

MIF, CD74 and other partners in kidney disease: Tales of a promiscuous couple

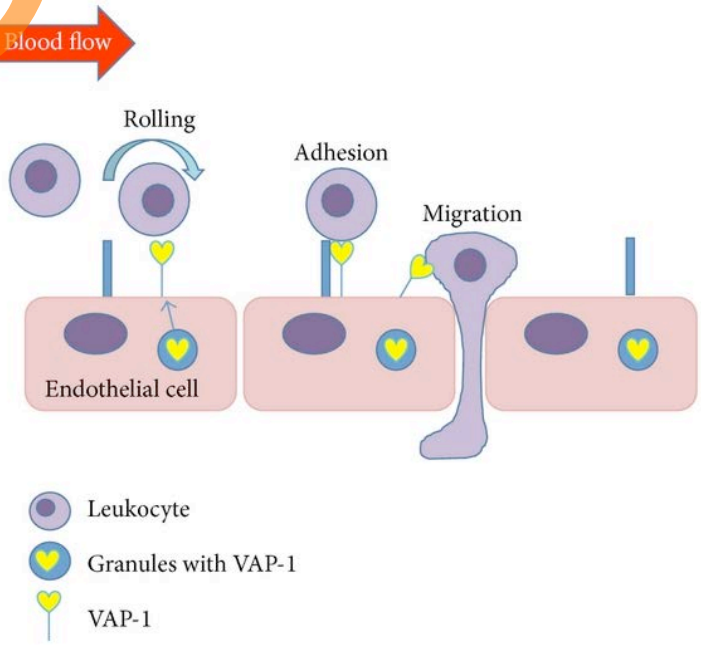
M.D. Sanchez-Niño [a,1], A.B. Sanz [a,1], O. Ruiz-Andres [b,2], J. Poveda [b,2], M.C. Izquierdo [b,2], R. Selgas [a,3], J. Egido [b,c,d,4], A. Ortiz [b,c,d,*]

VAP-1 inhibitor

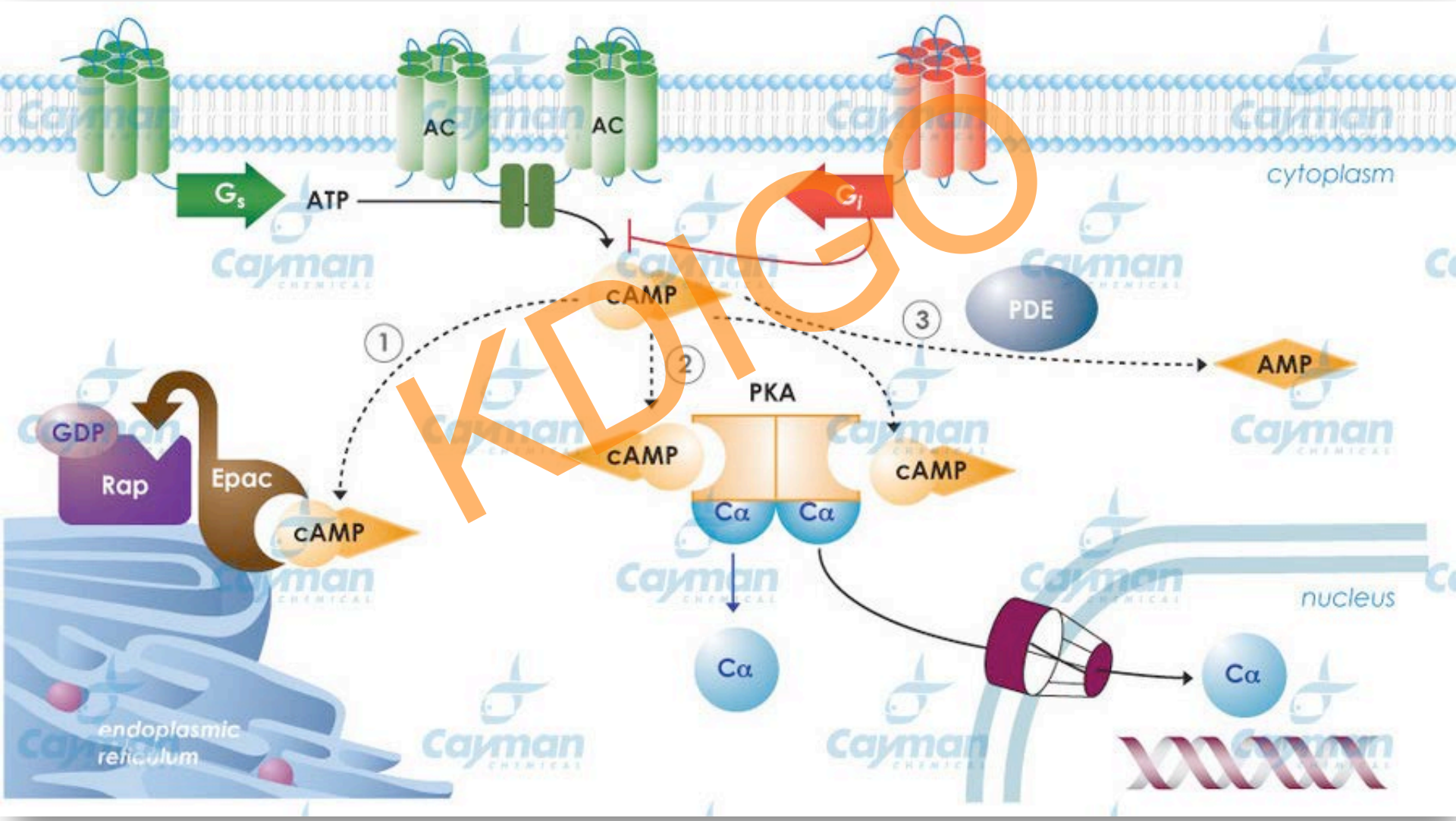
- VAP-1 is expressed in pericytes and vascular endothelium and is involved in leukocyte extravasation to inflammed tissues
- It is an enzyme (monoamine oxidase) and an adhesion molecule for lymphocytes.

ASP8232 – a novel VAP-1 inhibitor

Phase 1 clinical trial, oral drug
NCT02218099



Second messengers



CLINICAL RESEARCH www.jasn.org

February 2015, 26 (2)

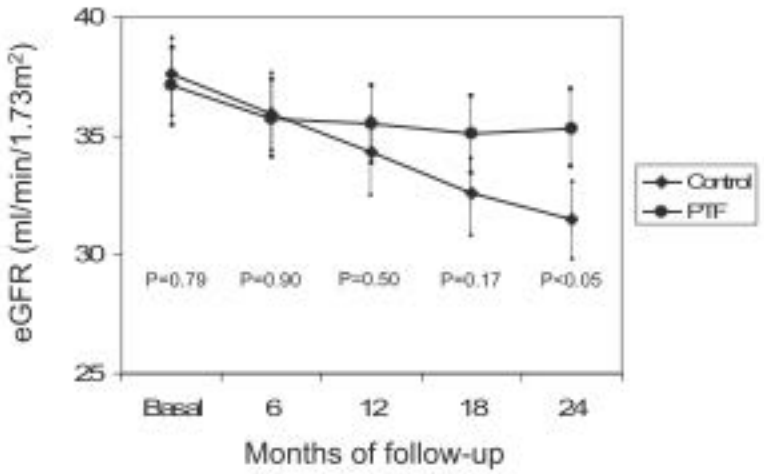
Effect of Pentoxifylline on Renal Function and Urinary Albumin Excretion in Patients with Diabetic Kidney Disease: The PREDIAN Trial

Juan F. Navarro-González,*†‡ Carmen Mora-Fernández,†‡ Mercedes Muros de Fuentes,‡§ Jesús Chahin,* María L. Méndez,* Eduardo Gallego,* Manuel Macía,* Nieves del Castillo,* Antonio Rivero,* María A. Getino,* Patricia García,* Ana Jarque,* and Javier García*

*Nephrology Service, †Research Unit, §Clinical Analysis Service, and ‡GEENDIAB (Spanish Group for the Study of Diabetic Nephropathy), University Hospital Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain

Open-label, prospective RCT
n=169, PTF 82, control 87

- smaller decrease in eGFR and a greater reduction of residual albuminuria.
- Reduction in TNF alpha



cAMP preservation – PDE inhibitors

Hypertension, 2009

Phosphodiesterase-5

Blood Pressure Lowering Effects of a New Long-Acting Inhibitor of Phosphodiesterase 5 in Patients With Mild to Moderate Hypertension

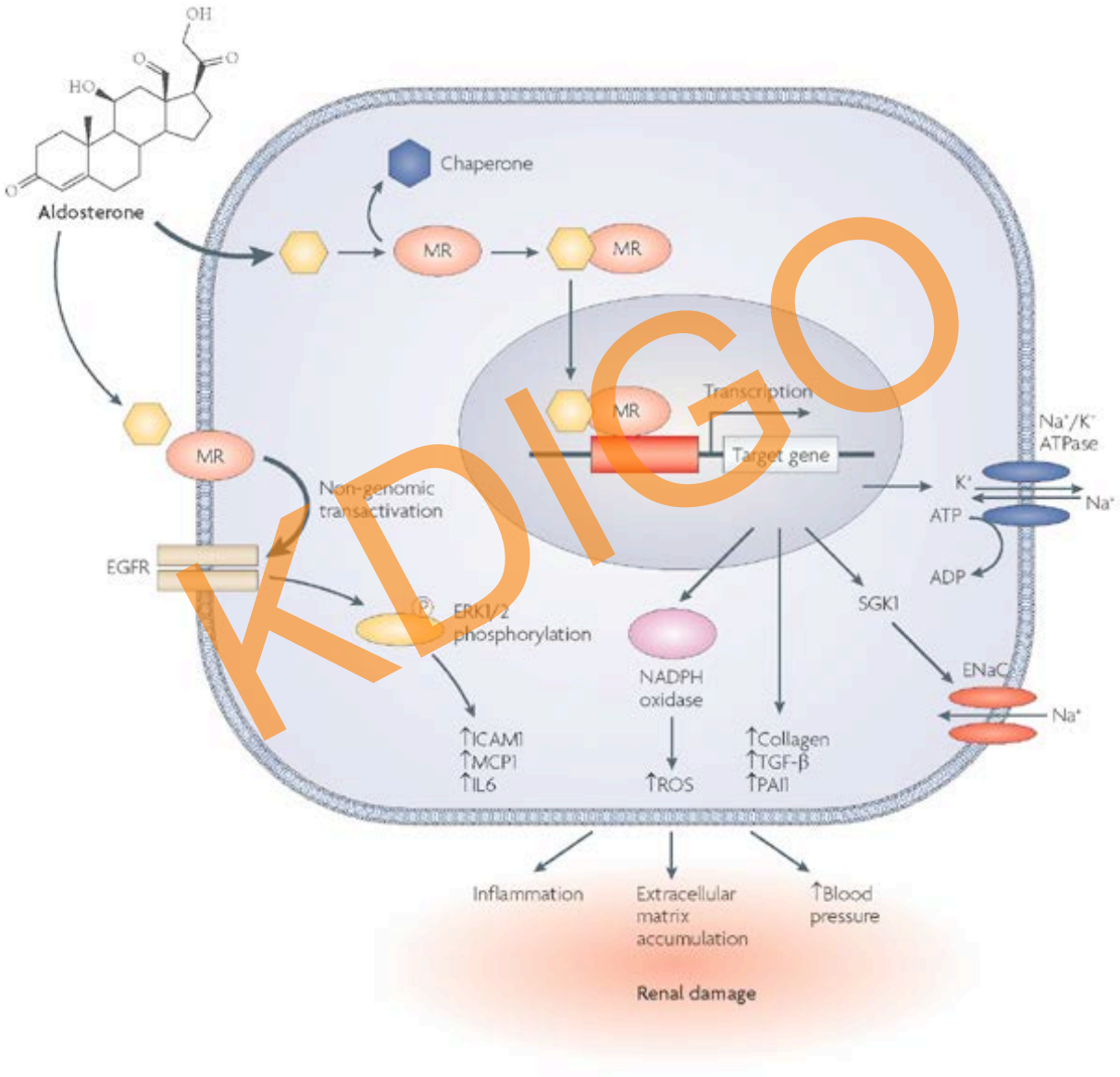
Robert Wolk, William B. Smith, Joel M. Neutel, John Rubino, Dawei Xuan, James Mancuso, James Gilbert, Milton L. Pressler

  - Blood vessel relaxation, improved blood flow
  - Phase 2, NCT01200394
- Finished phase 2a, 16 weeks, UACR, eGFR

cAMP – PDE inhibitors

- CTP-499
  - PDE3,4 and 5
  - Concert pharma
  - Poster, Phase 1, phase 2 active in Type 2 CKD, abstract NKF spring meeting
- Roflumolast (Takeda GmbH), Daliresp
  - PDE4
  - Approved for COPD
  - Preclinical efficacy in STNX model of CKD

Intracellular steroid receptors



Perico et al., Nat Rev Drug Disc 2008

BAY 94-8862 - Finerenone

Discovery of BAY 94-8862: A Nonsteroidal Antagonist of the Mineralocorticoid Receptor for the Treatment of Cardiorenal Diseases

Dr. Lars Bärfacker[1,*], Dr. Alexander Kuhl[1], Prof. Dr. Alexander Hillisch[1], Dr. Rolf Grosser[1], Dr. Santiago Figueroa-Pérez[1], Dr. Heike Heckroth[1], Adam Nitsche[1], Dr. Jens-Kerim Ergüden[1], Dr. Heike Gielen-Haertwig[1], Dr. Karl-Heinz Schlemmer[2], Prof. Dr. Joachim Mittendorf[1], Dr. Holger Paulsen[1], Dr. Johannes Platzek[3] and Dr. Peter Kolkhof[4]

Issue

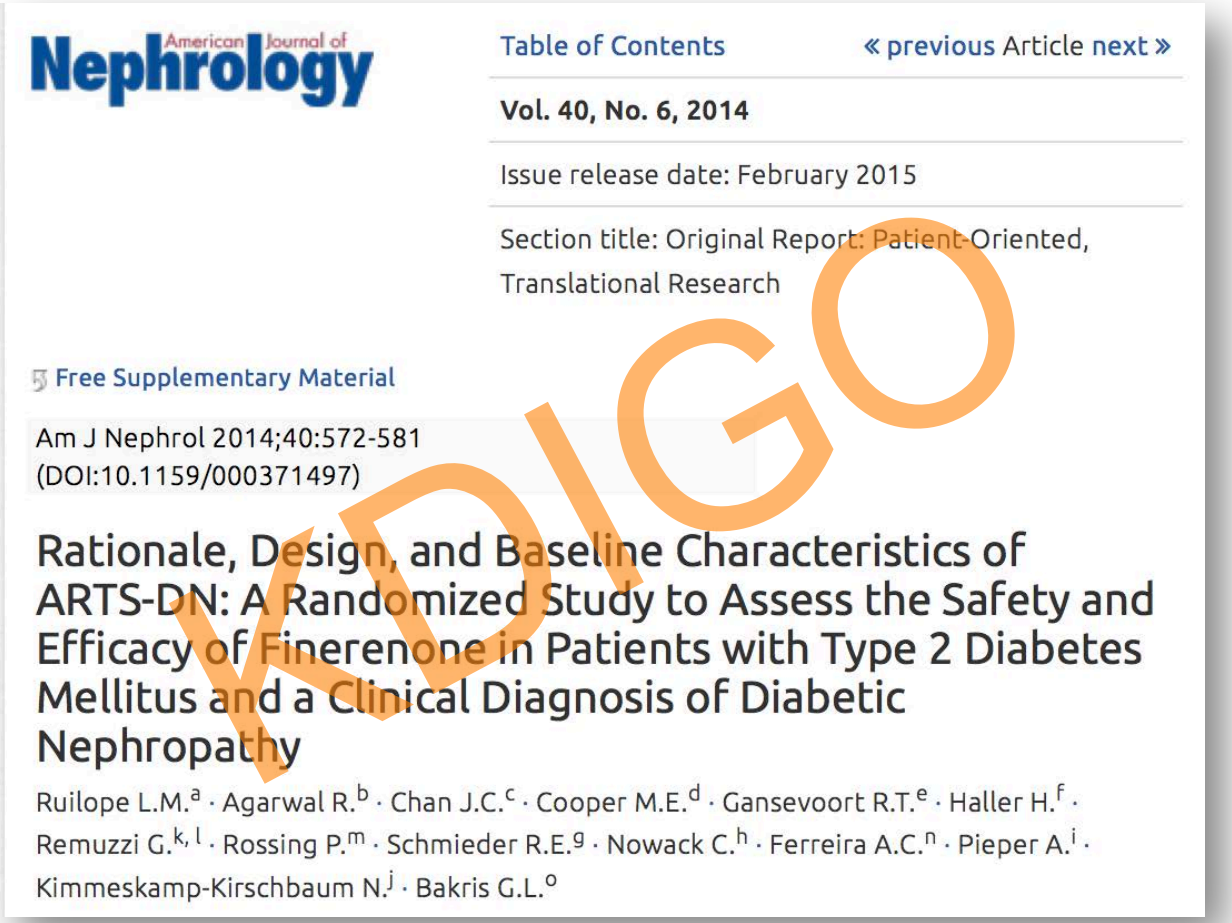
ChemMedChem

Volume 7, Issue 8, pages 1385–1403, August 2012

Article first published online: 12 JUL 2012

DOI: 10.1002/cmdc.201200081

BAY 94-8862 - Finerenone



American Journal of Nephrology

Table of Contents « previous Article next »

Vol. 40, No. 6, 2014

Issue release date: February 2015

Section title: Original Report: Patient-Oriented, Translational Research

Free Supplementary Material

Am J Nephrol 2014;40:572-581
(DOI:10.1159/000371497)

Rationale, Design, and Baseline Characteristics of ARTS-DN: A Randomized Study to Assess the Safety and Efficacy of Finerenone in Patients with Type 2 Diabetes Mellitus and a Clinical Diagnosis of Diabetic Nephropathy

Ruilope L.M.[a] · Agarwal R.[b] · Chan J.C.[c] · Cooper M.E.[d] · Gansevoort R.T.[e] · Haller H.[f] · Remuzzi G.[k, l] · Rossing P.[m] · Schmieder R.E.[g] · Nowack C.[h] · Ferreira A.C.[n] · Pieper A.[i] · Kimmeskamp-Kirschbaum N.[j] · Bakris G.L.[o]

ARTS-DN; NCT01874431

Mineralocorticoid receptors.. MT-3995

Mitsubishi Tanabe Pharma

Safety, Tolerability and Pharmacokinetic Study of MT-3995 at a Low Dose in Subjects With Diabetic Nephropathy

This study is currently recruiting participants. (see Contacts and Locations)

Verified July 2014 by Mitsubishi Tanabe Pharma Corporation

Sponsor:
Mitsubishi Tanabe Pharma Corporation

Information provided by (Responsible Party):
Mitsubishi Tanabe Pharma Corporation

ClinicalTrials.gov Identifier:
NCT02205372

First received: July 27, 2014
Last updated: July 30, 2014
Last verified: July 2014
History of Changes

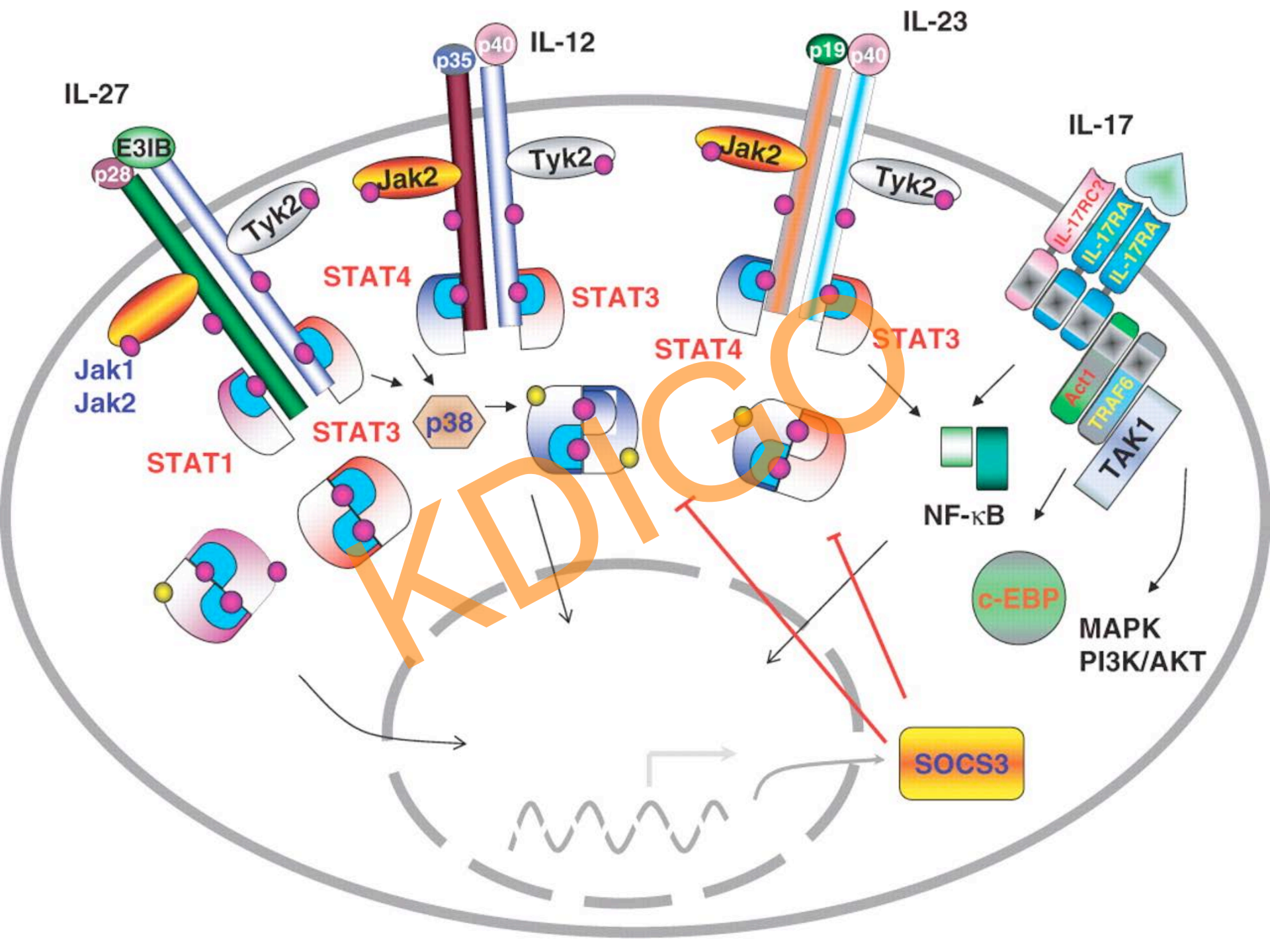
Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

The purpose of this study is to evaluate safety, tolerability and pharmacokinetics of **MT-3995** in Subjects with Diabetic Nephropathy.

Condition	Intervention	Phase
Diabetic Nephropathy	Drug: **MT-3995** Drug: Placebo	Phase 1 Phase 2

Inflammatory cytokine cascade
JAK-STAT pathway inhibitors


IL-27
E3IB
p28
Tyk2
Jak1
Jak2
STAT1
STAT3
IL-12
p35
p40
Jak2
Tyk2
STAT4
STAT3
p38
IL-23
p19
p40
Jak2
Tyk2
STAT4
STAT3
IL-17
IL-17RC?
IL-17RA
IL-17RA
Act1
TRAF6
TAK1
NF-κB
c-EBP
MAPK
PI3K/AKT
SOCS3
KDIGO

Stat-4 antagonist

- DiaKine – oral drug, DT 22669
- JAK Tyrosine kinases
- Acquired by Islet Sciences, interest in prevention of islet cell senescence
- preclinical studies failed to prevent rodent diabetes

- Retinopathy/nephropathy DT 23552

JAK1/JAK2 inhibitor *baricitinib*

- Oral agent
- Phase III development as a potential treat
  rheumatoid arthritis.

Lilly

This study has been completed.

Sponsor:
Eli Lilly and Company

Collaborator:
Incyte Corporation

Information provided by (Responsible Party):
Eli Lilly and Company

ClinicalTrials.gov Identifier:
NCT01683409

First received: September 7, 2012
Last updated: January 16, 2015
Last verified: January 2015
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

This is a dose ranging study to evaluate the safety and efficacy of **baricitinib** in the treatment of participants with mild to moderate diabetic kidney disease.

Condition	Intervention	Phase
Diabetic Kidney Disease	Drug: **baricitinib** Drug: Placebo	Phase 2

Aerpio

- Tie2Rec activator – angiopoietin receptor, tyrosine kinase inhibitor

BASIC RESEARCH www.jasn.org

Targeted Glomerular Angiopoietin-1 Therapy for Early Diabetic Kidney Disease

Cecile Dessapt-Baradez,* Adrian S. Woolf,† Kathryn E. White,‡ Jiaqi Pan,* Jennifer L. Huang,§ Anthea A. Hayward,* Karen L. Price,§ Maria Kolatsi-Joannou,§ Maelle Locatelli,* Marine Diennet,* Zoe Webster,‖ Sarah J. Smillie,* Viji Nair,¶ Matthias Kretzler,¶ Clemens D. Cohen,** David A. Long,§ and Luigi Gnudi*

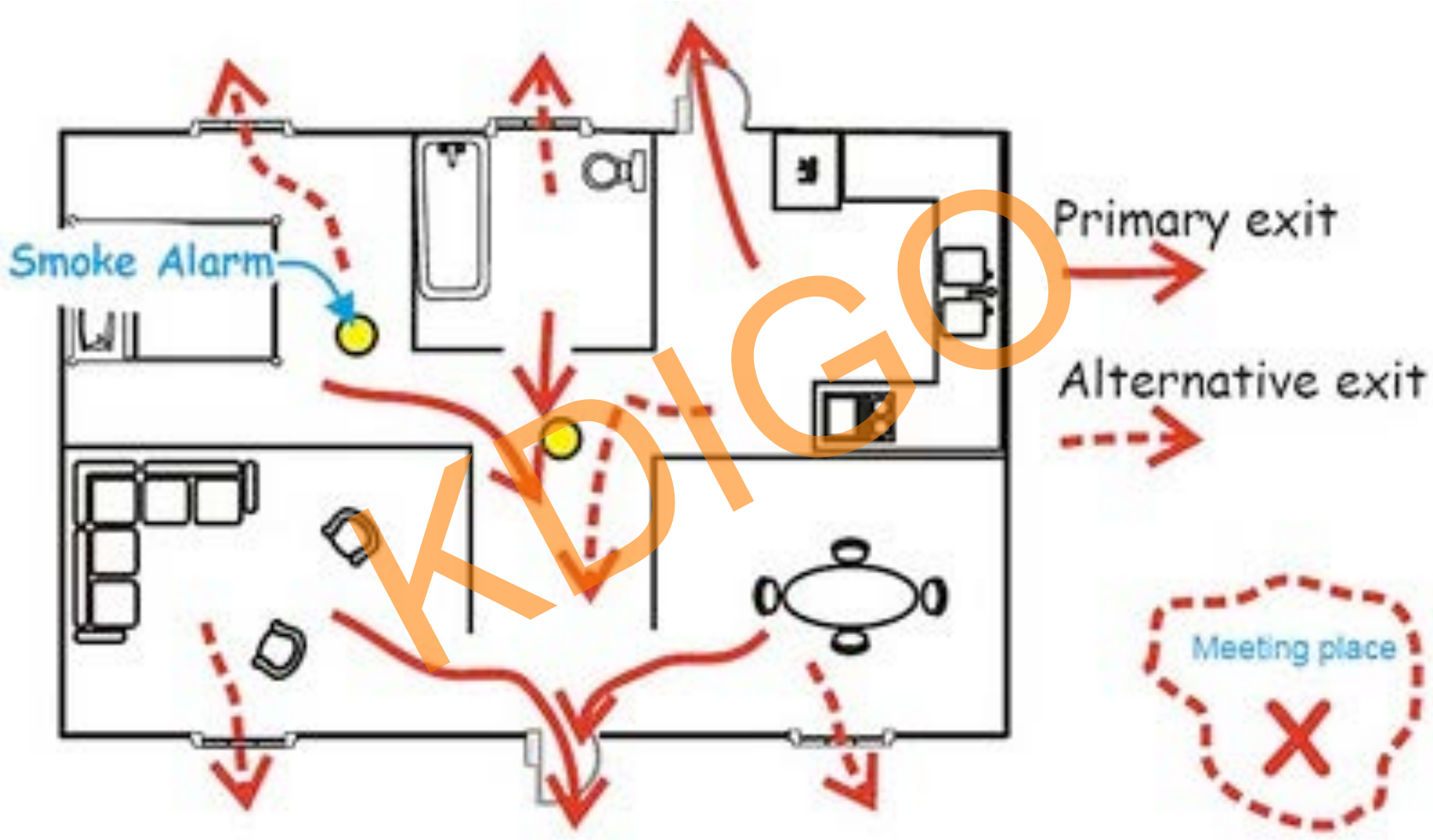
*Cardiovascular Division, King's College London, London, United Kingdom; †Institute of Human Development, Faculty of Medical and Human Sciences, University of Manchester, Manchester, United Kingdom; ‡Electron Microscopy Unit, University of Newcastle upon Tyne, Newcastle upon Tyne, United Kingdom; §Nephro-Urology Unit, University College London, Institute of Child Health, London, United Kingdom; ‖MRC CRB, ICSM Hammersmith Hospital, Imperial College London, London, United Kingdom; ¶Internal Medicine/Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, Michigan; and **Division of Nephrology, University Hospital Zurich, Zurich, Switzerland

The dilemma…

- Multiple pathways
- Risk of redundancy when one pathway is blocked

- IPF an epithelial-fibroblastic disease – inflammation is a secondary event

Understanding disease pathophysiology – network analysis



VAP-1 inhibitor

A Study to Evaluate ASP8232 in Reducing Central Retinal Thickness in Subjects With Diabetic Macular Edema (DME) (VIDI)

This study is currently recruiting participants. (see Contacts and Locations)

Verified January 2015 by Astellas Pharma Inc

Sponsor:
Astellas Pharma Europe B.V.

Information provided by (Responsible Party):
Astellas Pharma Inc (Astellas Pharma Europe B.V.)

ClinicalTrials.gov Identifier:
NCT02302079

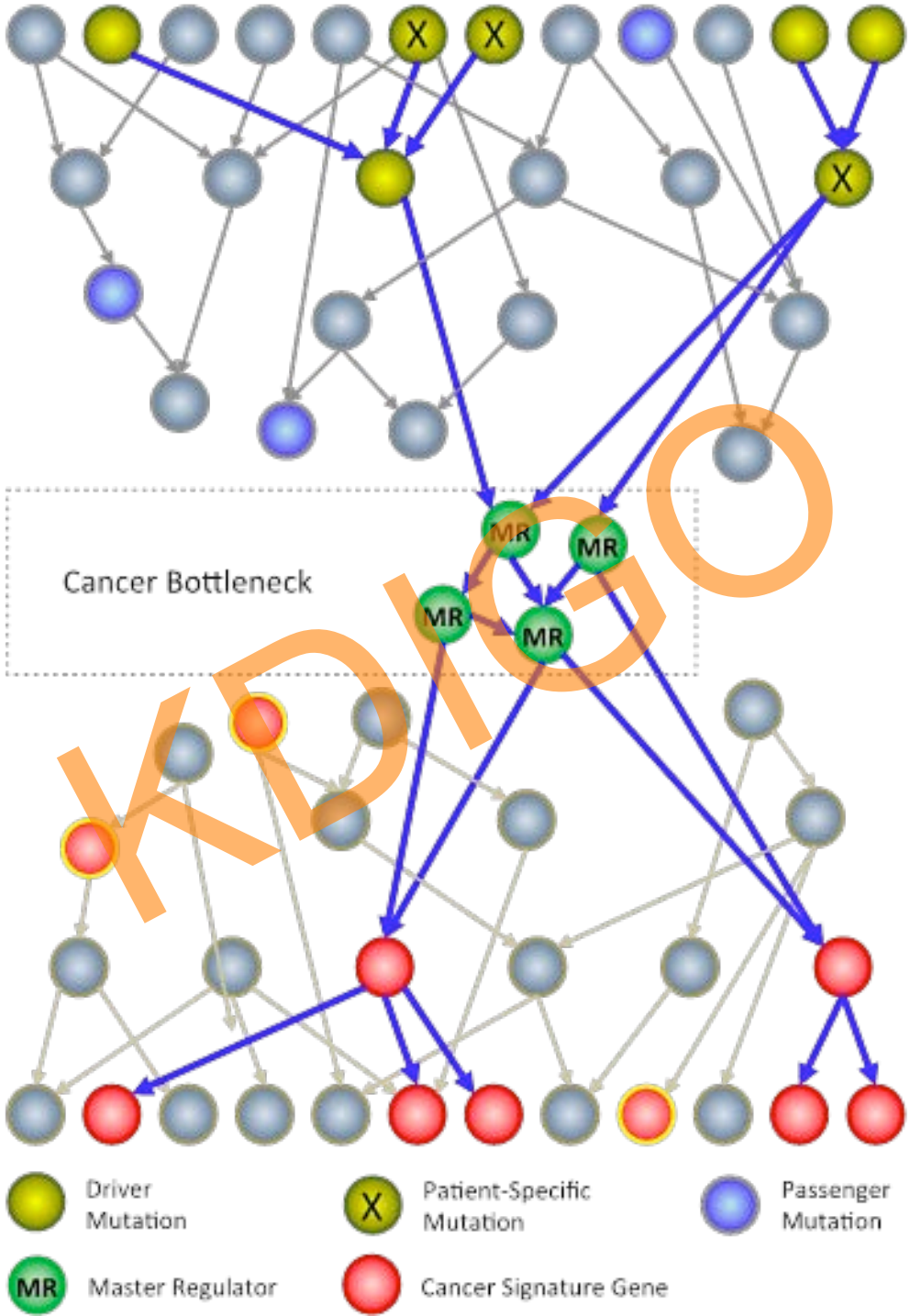
First received: November 24, 2014
Last updated: January 30, 2015
Last verified: January 2015
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

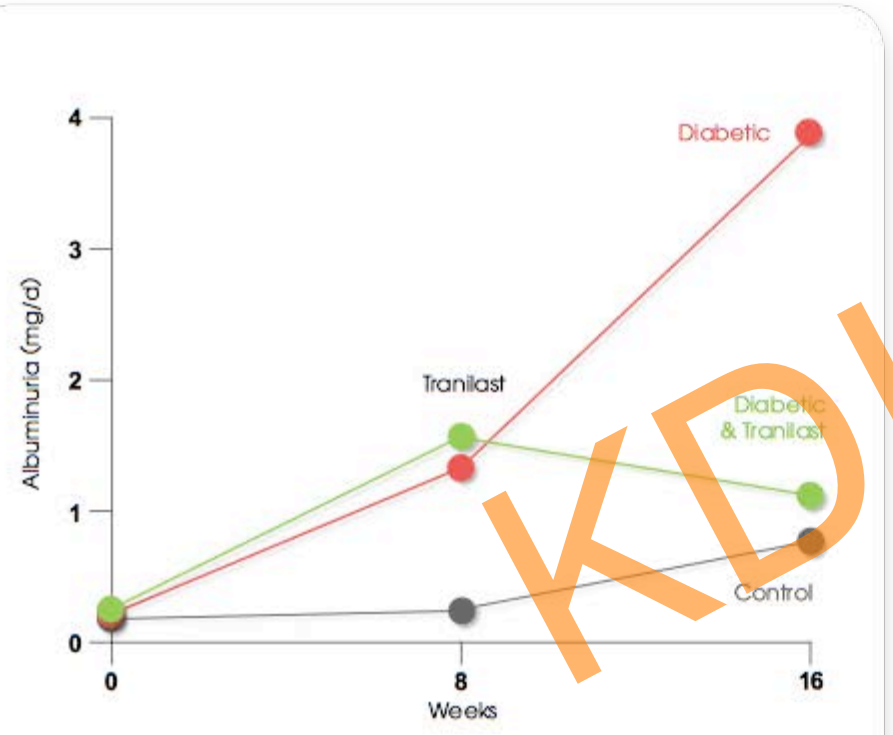
Purpose

The purpose of this study is to evaluate efficacy and safety of **ASP8232** in subjects with diabetic macular edema (DME). This study will evaluate the percent change from baseline in excess central subfield thickness (CST) in the study eye as assessed by spectral domain-optical coherence Tomography (SD-OCT) for **ASP8232** monotherapy at Month 3.

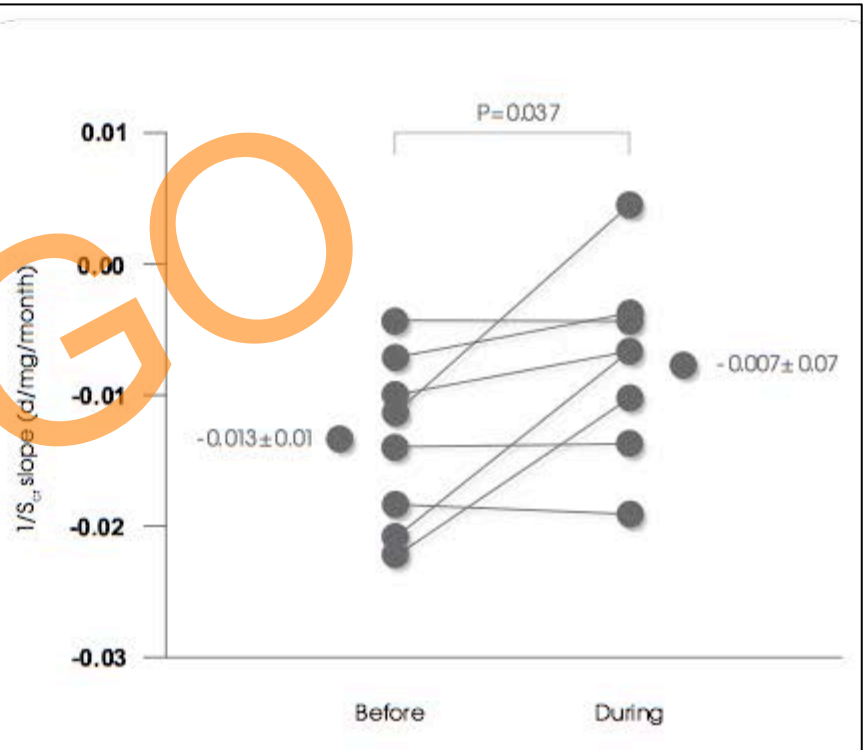
Condition	Intervention	Phase
Diabetes Mellitus Diabetic Macular Edema	Drug: **ASP8232** Drug: ranibizumab Drug: Placebo Other: Sham intravitreal (IVT) injection	Phase 2


X
X
X
MR
MR
MR
MR
Cancer Bottleneck
Driver Mutation
Patient-Specific Mutation
Passenger Mutation
MR
Master Regulator
Cancer Signature Gene

Tranilast – a known but old anti-fibrotic



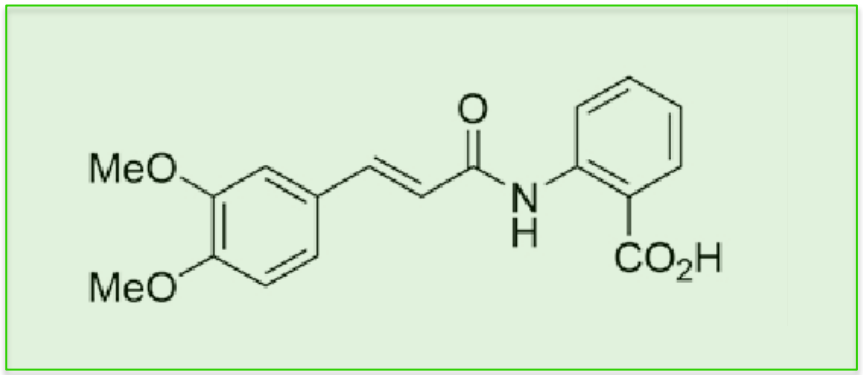
Tranilast halts the progression of albuminuria in diabetic Ren-2 rats



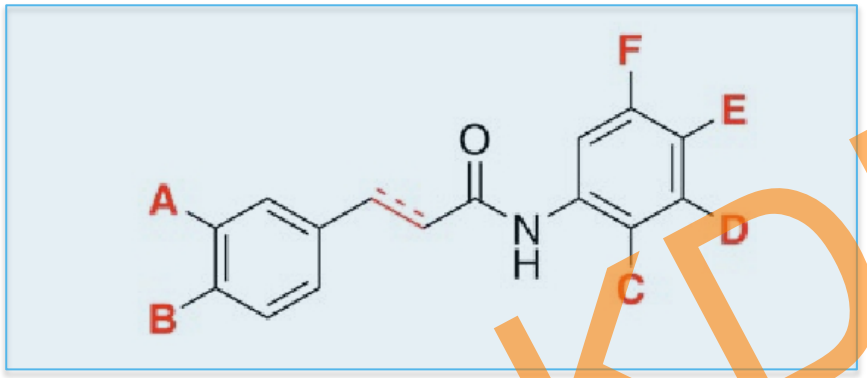
Tranilast slows the progression of diabetic nephropathy in humans (100mg/day TID)

A. Mifsud et al, Nephron Physiol 2003

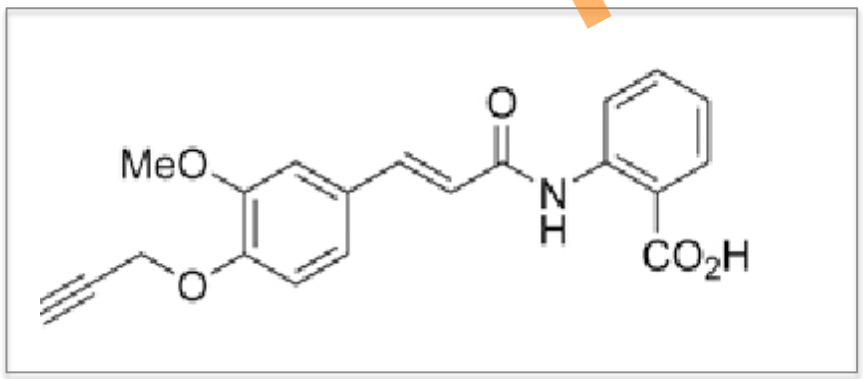
B. Soma et al., Nephron 2002



Tranilast



Fibrotech compounds



FT-011

Tranilast
n-(3,4-dimethyoxycinnamoyl) anthranilic acid

>130 Fibrotech compounds

Lead compound – FT-011

- Novel, synthesized on a kilogram scale, orally bioavailable, stable and crystalline.
- CMC – AMRI, New York

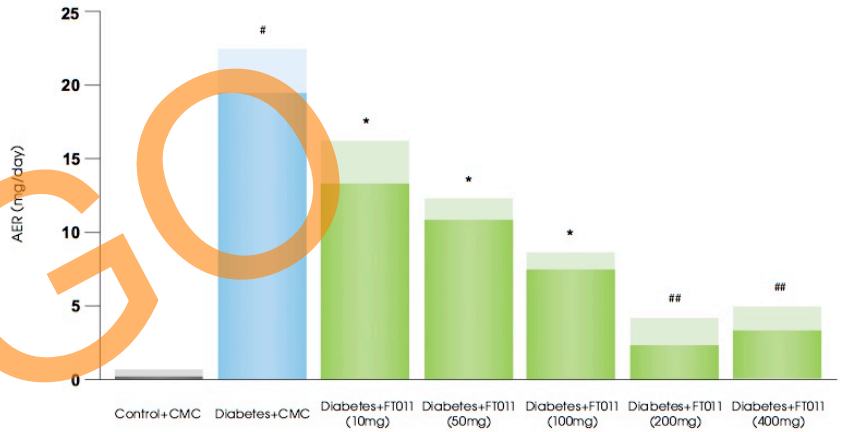
Extensive preclinical studies, at 50-1000mg/kg/day with no aberrant pathology seen in any organ, normal FBE, normal renal function. FT-011 better tolerability than Tranilast

Preclinical studies – FT011 and DN

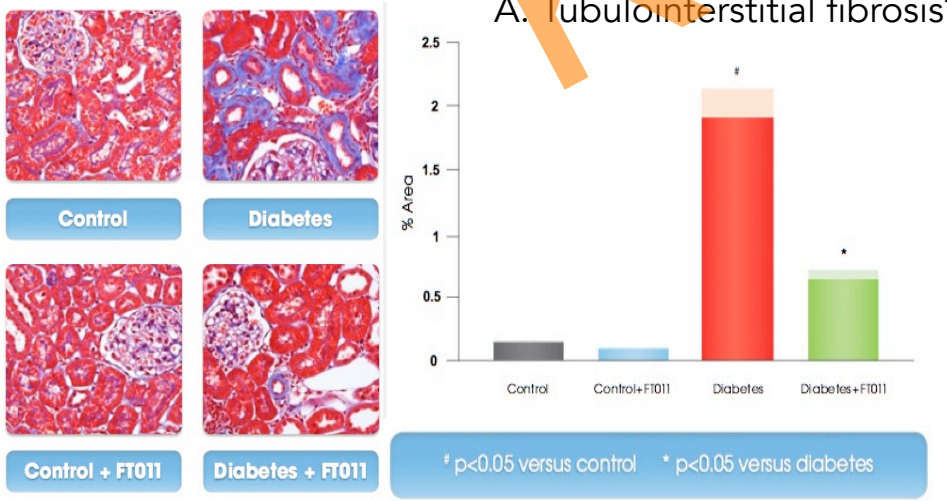
FT011 has been studied in the Ren(2) diabetic rat, and other STZ rat models with both early and later intervention demonstrating a dose dependant reduction in urinary ACR, reduction in tubulo-interstitial fibrosis, glomerulosclerosis and abrogation of GFR decline. (*Gilbert et al, PLoS One, 2012). Efficacy has also been demonstrated in the STNx model of CKD.

In head to head studies, FT011 has been demonstrated to be more potent than tranilast

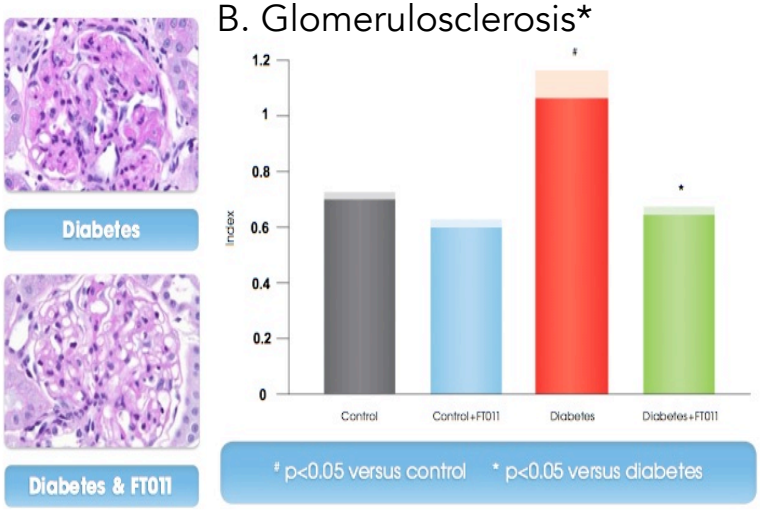
Dose dependant reduction in urinary ACR



A. Tubulointerstitial fibrosis*



B. Glomerulosclerosis*



Phase 1 clinical trial summary

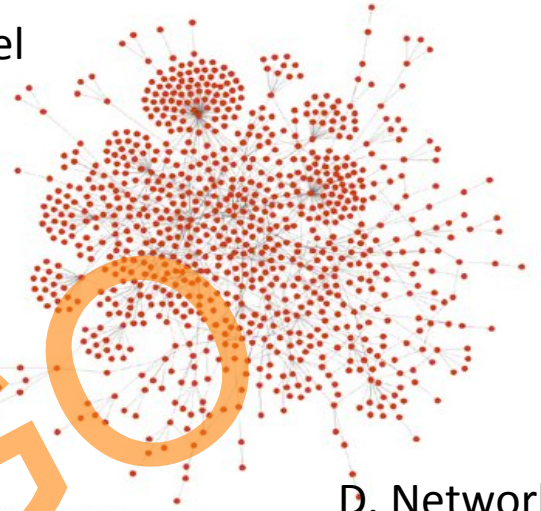
- FT011 has been tested at up to 1gm as a single dose with no adverse effects
- FT011 dosed at 500mg/day for 14 day period with no adverse events
- FT011 has excellent PK with half life of ~10 hours

Systems Biology – Network analysis

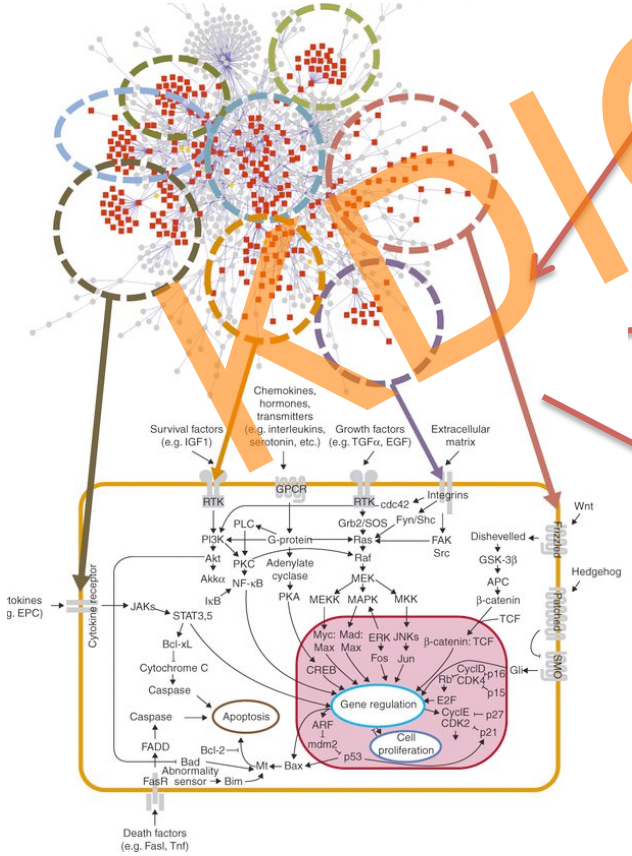
A. ‘Omic data

1. List of proteins, genes or metabolites from ‘omic data sets
2.
3.
4.

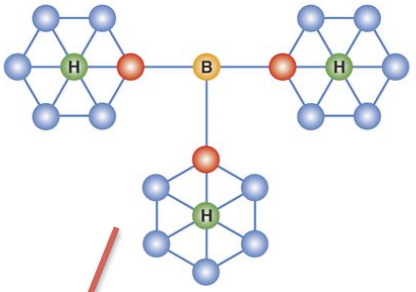
B. Interactome Model



C. Network Clusters

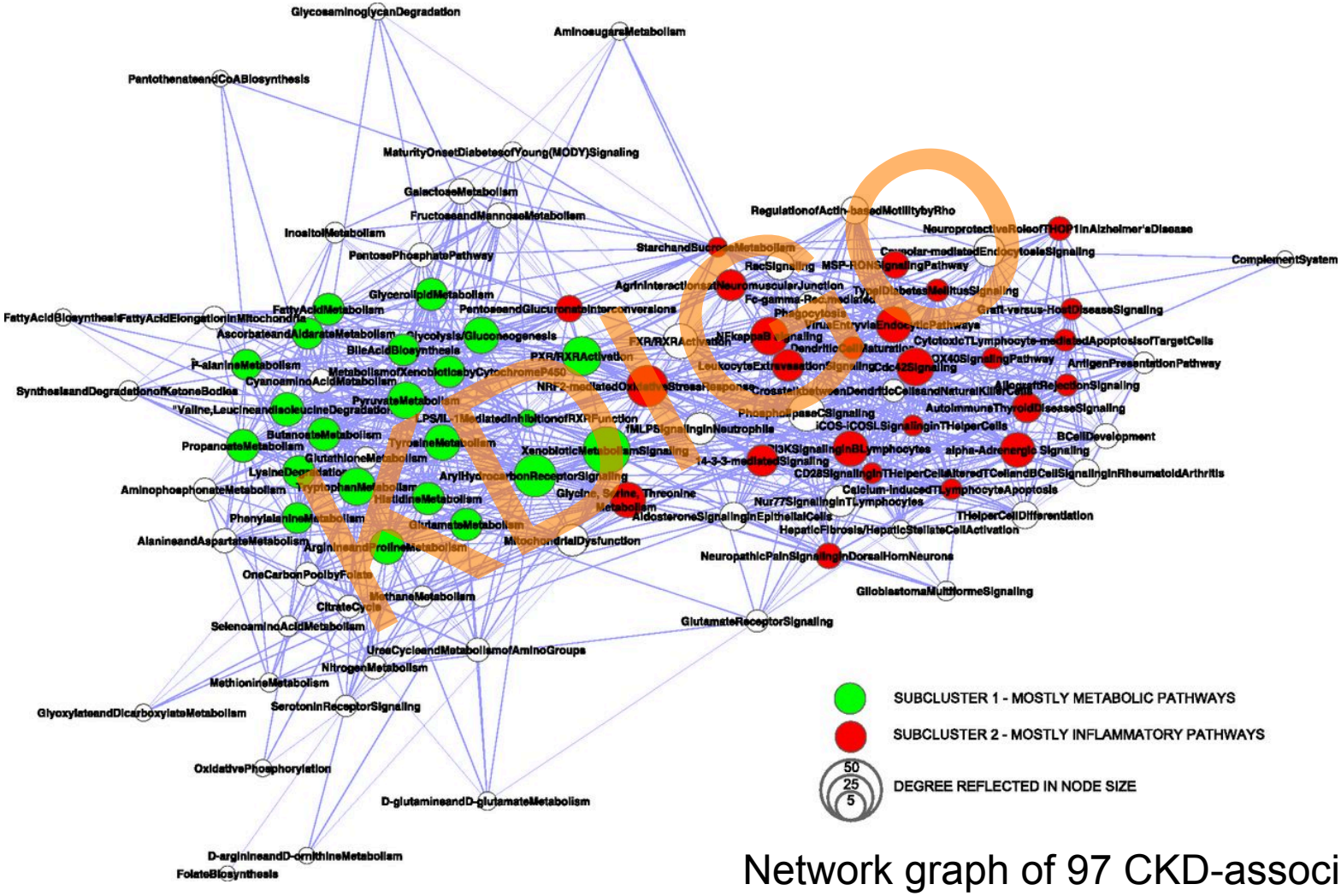


D. Network Topology



Function and Prioritisation

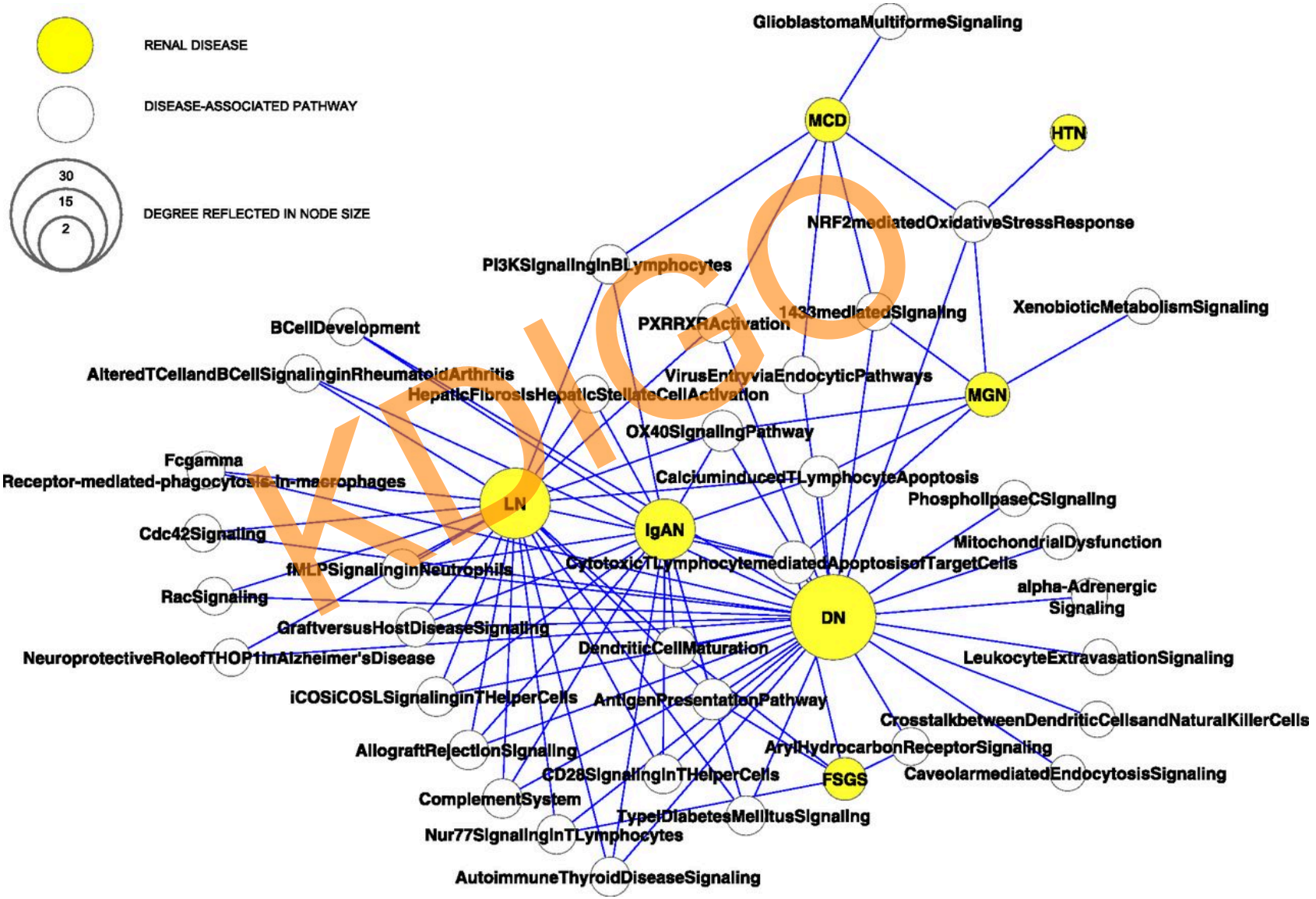
A comprehensive pathway map of CKD.



Network graph of 97 CKD-associated pathway nodes

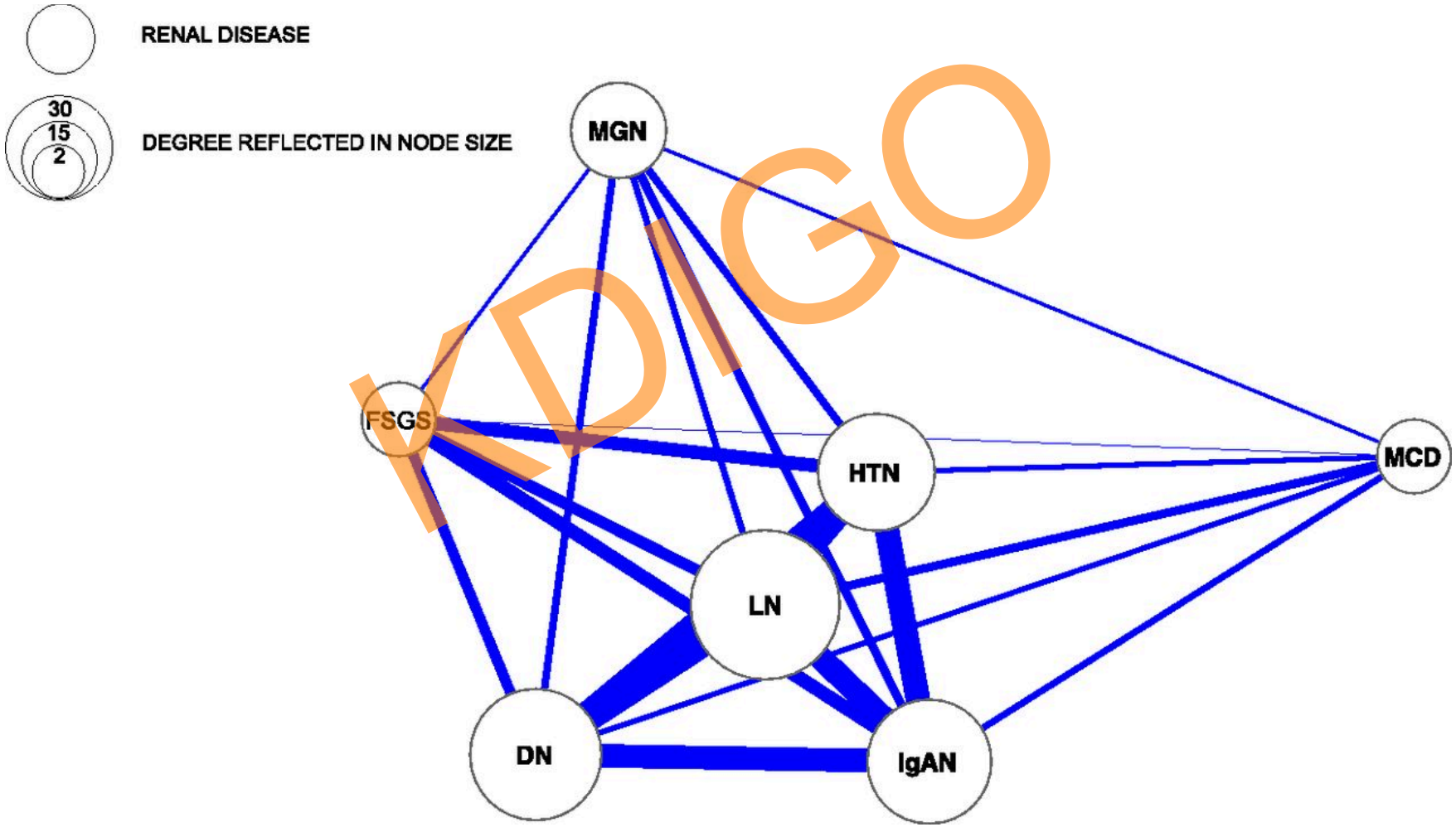
Martini S et al. JASN 2013

CKD associated pathways are shared between renal diseases.



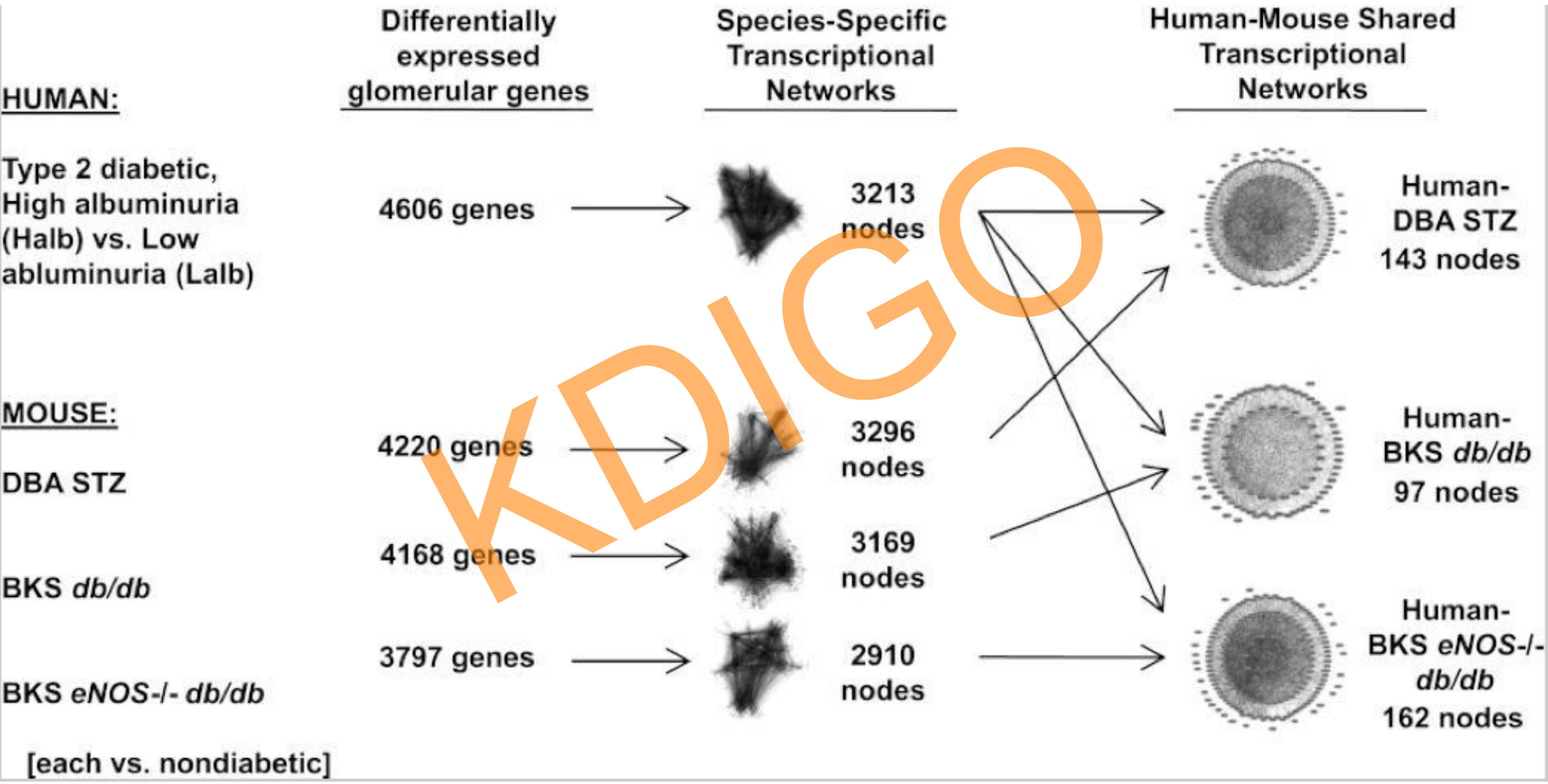
Martini S et al. JASN 2013

Disease-specific analyses shows a close interconnection between lupus nephritis, IgA nephritis, and diabetic nephropathy.



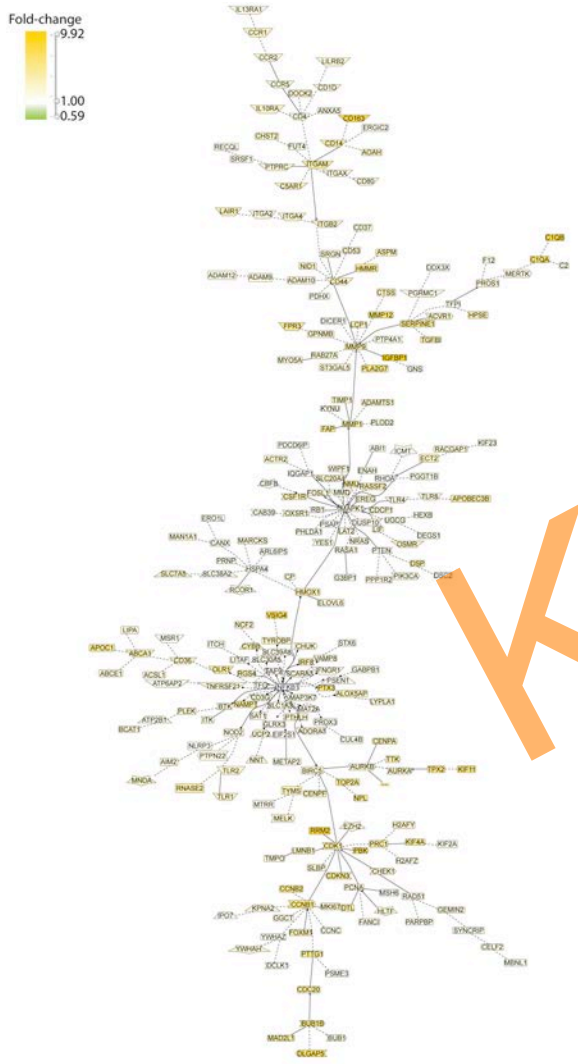
Martini S et al. JASN 2013

Identification of Cross-Species Shared Transcriptional Networks of Diabetic Nephropathy in Human and Mouse Glomeruli



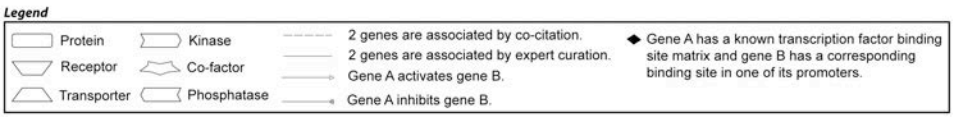
Hodgin et al, Diabetes 2013

The Molecular Phenotype of Endocapillary Proliferation: Novel Therapeutic Targets for IgA Nephropathy



Canonical pathways (number of genes regulated/number of genes in the pathway)	p-value	Regulated molecules in the pathway
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses (14/106)	0.0000	PTX3,TLR1,PIK3CA,NLRP3,MAPK1,TLR8, C1QA,C1QB,EIF2S1,TLR2,TLR4,NOD2, C5AR1, PRKD3
Leukocyte Extravasation Signaling (18/201)	0.0001	PIK3CA,MAPK1,ITGA2,BTK,ITGB2,WIPF1, ITGAM,TIMP1,RHOA,NCF2,CD44,CYBB, MMP12,PRKD3,MMP9,MMP1,ITGA4,ITK
TREM1 Signaling (9/71)	0.0001	TLR2,TLR4,TLR1,NOD2,MAPK1,TYROBP, TLR8,LAT2,ITGAX
NF-κB Activation by Viruses (10/82)	0.0003	ITGB2,PIK3CA,CCR5,NRAS,MAPK1,CD4, ITGA2,CHUK,PRKD3,ITGA4
Toll-like Receptor Signaling (8/62)	0.0004	TLR2,TLR4,TLR1,MAPK1,MAP3K7,TLR8, CD14,CHUK
Cell Cycle: G2/M DNA Damage Checkpoint Regulation (7/48)	0.0006	YWHAH,YWHAZ,TOP2A,CCNB2,CDK1, CHEK1,CCNB1
IL-8 Signaling (16/205)	0.0006	PIK3CA,NRAS,MAPK1,IQGAP1,RAB11FIP2, ITGB2,HMOX1,ITGAM,RHOA,NCF2,CYBB, CHUK,PRKD3,GNG12,MMP9,ITGAX
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages (13/210)	0.0089	PIK3CA,MAPK1,IFNGR1,TLR2,APOC1,TLR4, MAP3K7,RHOA,NCF2,CYBB,IRF8,CHUK, PRKD3

Selected canonical pathways significantly regulated (p-value<0.05) from the 424 genes regulated in E1 vs. E0 biopsies, as assessed by Ingenuity Pathway Analysis. Full pathway list in Table S3.
doi:10.1371/journal.pone.0103413.t003

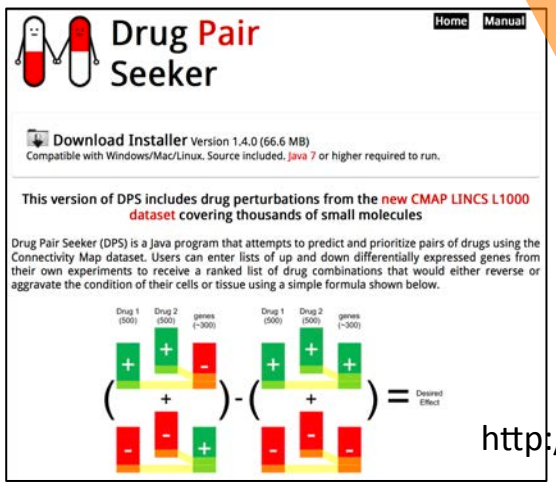


Hodgin et al, PlosOne 2014

The Molecular Phenotype of Endocapillary Proliferation: Novel Therapeutic Targets for IgA Nephropathy

Rank	Cmap name	p
1	Hydroquinine	0.0002
3	Resveratrol	0.0003
8	guaifenesin	0.0016
10	methotrexate	0.0025
12	genistein	0.0061
24	ciclosporin	0.0148
64	corticosterone	0.0324
72	methylprednisolone	0.0405

These are bioactive compounds that would be predicted to have favorable biologic activity to modulate the transcriptional responses associated with endocapillary proliferation. Full results of the analysis are available in Table S6.
doi:10.1371/journal.pone.0103413.t004

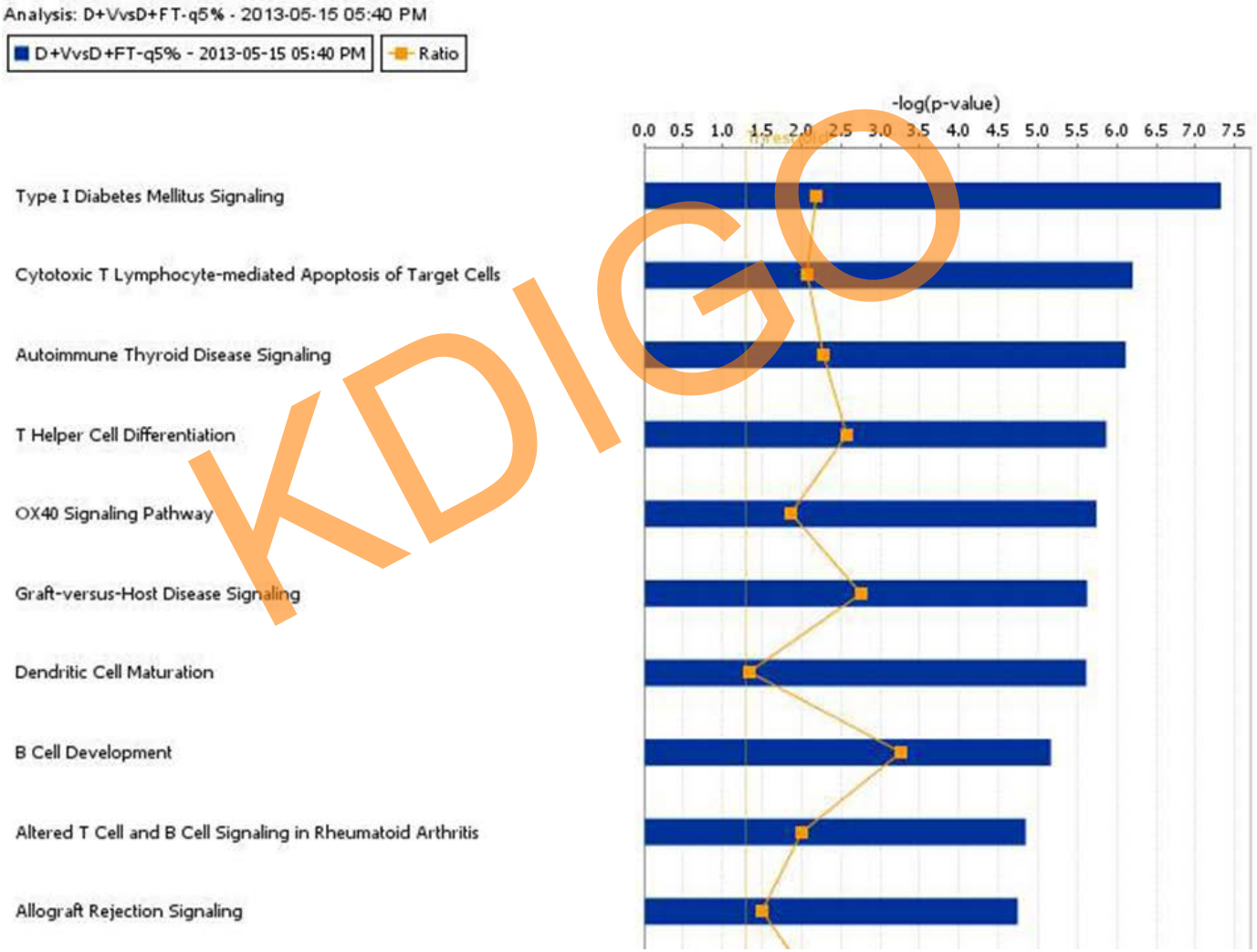


- Defined distinct molecular profile of a pathologic phenotype associated with progressive renal insufficiency in IgAN.
- Identification of new therapeutic strategies for IgAN.

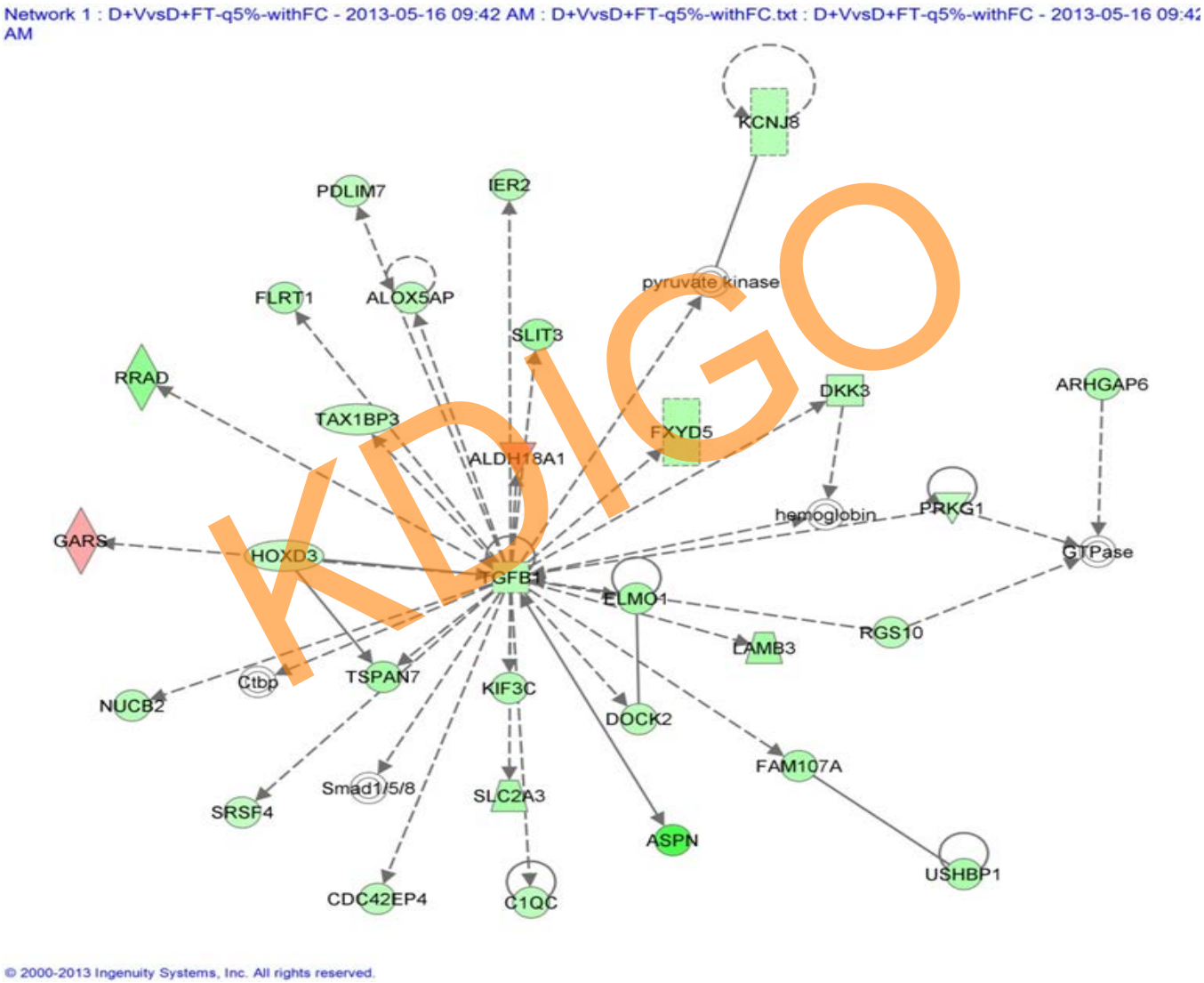
http://www.maayanlab.net/DPS/

Hodgin et al, PlosOne 2014

Top 10 pathways differentially regulated by FT011 in treated and untreated diabetic animals.



Network analysis of FT011 pathway mechanisms



7 of 10 pathways common in human and animal DN is are affected by FT011

New therapies - ?the future

- Return to the renal biopsy
  - Pharmacotranscriptomics
- Alternate dosing schedules
  - Rest periods, prevent saturation/adaptation