Société de Physiologie

APFCN

SFNDT

Physiopathologie de l'acide urique

Hang Korng Ea

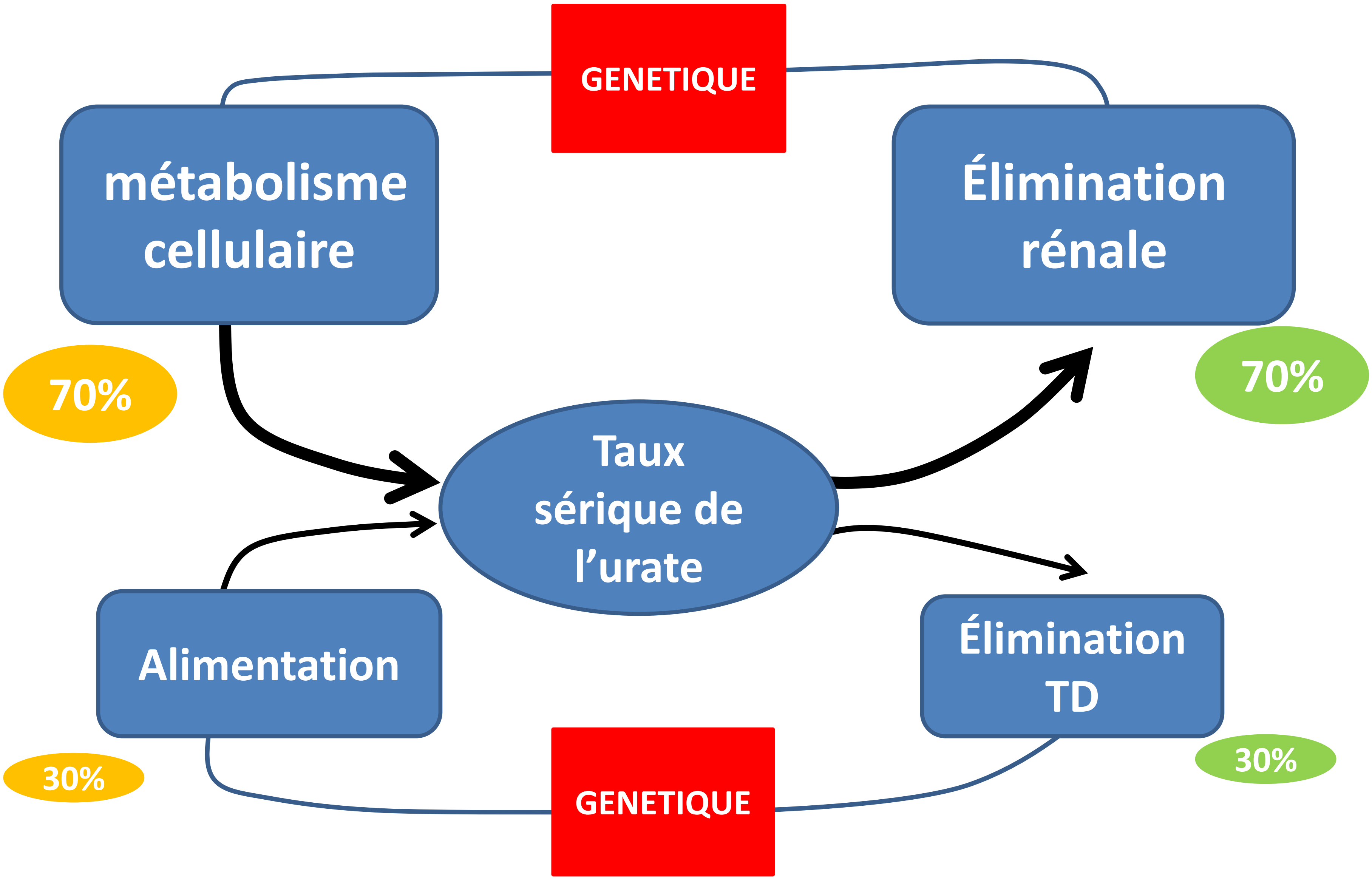
Hôpitaux Universitaires
SAINT-LOUIS
LARIBOISIÈRE
FERNAND-WIDAL

Alimentation et gène dans régulation de l’acide urique

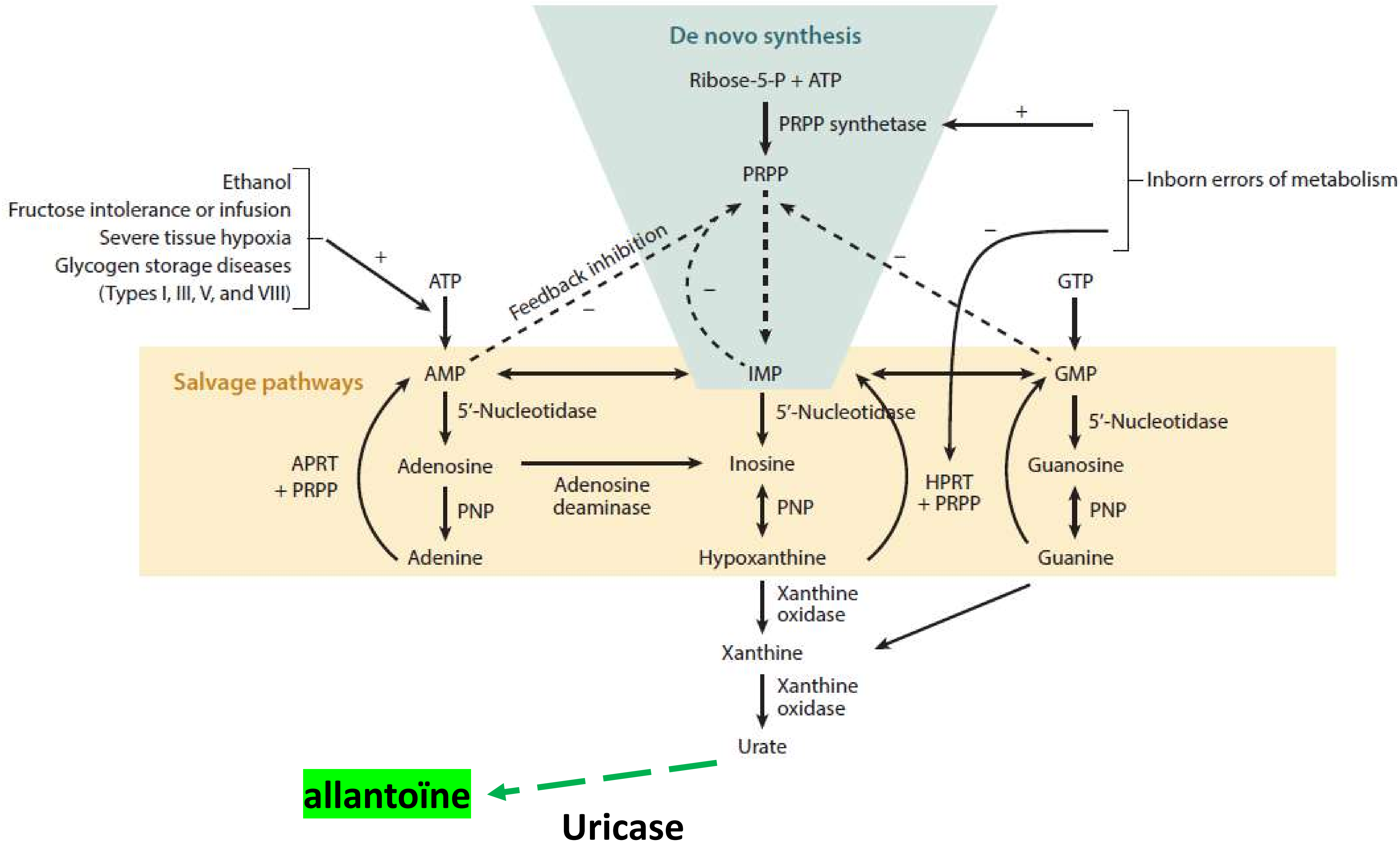
Régulation rénale

Régulation digestive

Hyperuricémie et goutte

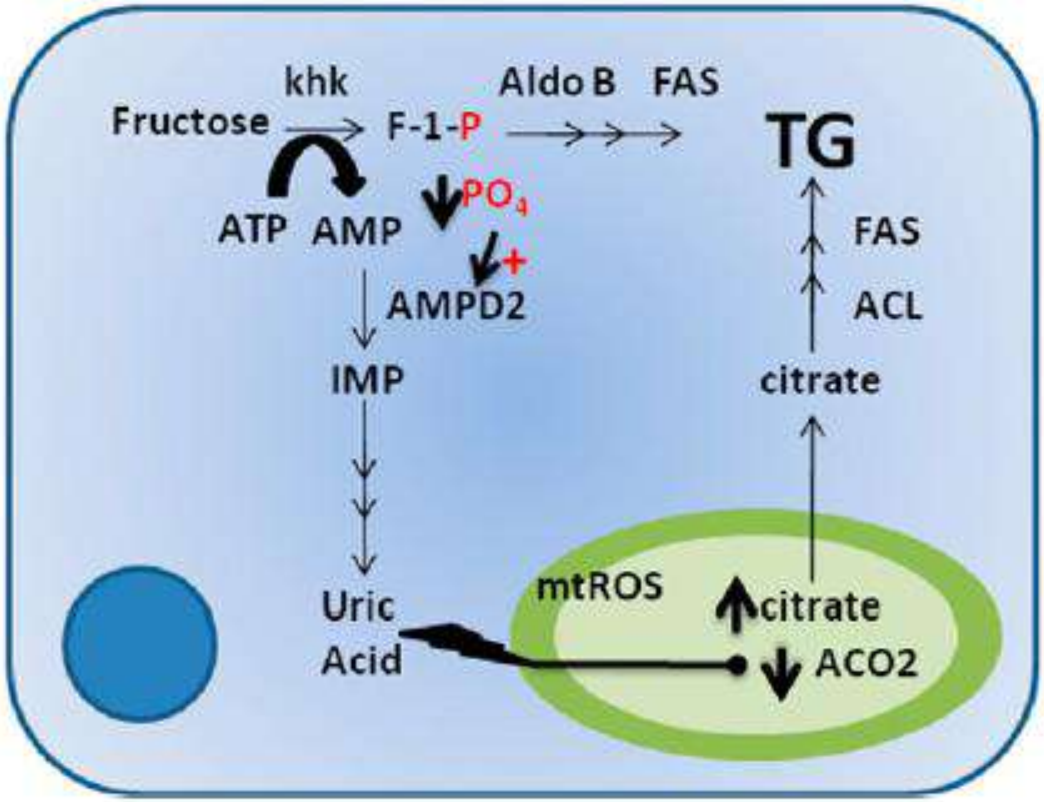

GENETIQUE
métabolisme cellulaire
Élimination rénale
70%
70%
Taux sérique de l'urate
Alimentation
Élimination TD
30%
30%
GENETIQUE

Acide urique : synthèse hépatique



Mandal 2015 Ann Rev Physiol

Uricémie et fructose



Johnson 2013 Diabetes

BMJ Open

2016

Fructose intake and risk of gout and hyperuricemia: a systematic review and meta-analysis of prospective cohort studies

Joseph Jamnik,[1] Sara Rehman,[1,2] Sonia Blanco Mejia,[1,2] Russell J de Souza,[2,3] Tauseef A Khan,[1,2] Lawrence A Leiter,[1,2,4,5,6] Thomas M S Wolever,[1,2,4,5,6] Cyril W C Kendall,[1,2,7] David J A Jenkins,[1,2,4,5,6] John L Sievenpiper[1,2,5,6]

Table 1 Characteristics of prospective cohort studies investigating total dietary fructose intake and incident gout

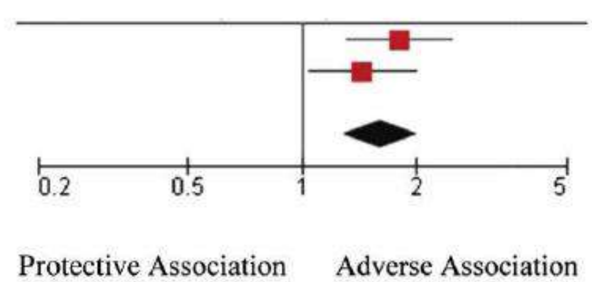
Study, year	Country	Participants	Age range	Duration	Dietary assessment	Divisions	Total incidence	Exposure range (total fructose)	Method of outcome measure	Funding source*	Adjustments
Choi *et al*,[38] 2008 Males	USA	46 393 M	40–75	12 years	Food frequency questionnaire (repeated every 4 years)	Quintiles	755	<6.9–>11.8 (% energy)	Self-report and supplementary questionnaire	Agency	Age, total energy intake, BMI, diuretic use, hypertension, renal failure, alcohol, vitamin C, percentage of energy from carbohydrates
Choi *et al*,[39] 2010 Females	USA	78 906 F	30–55	22 years	Food frequency questionnaire (repeated every 4 years)	Quintiles	778	<7.5–>11.9 (% energy)	Self-report and supplementary questionnaire	Agency	Age, total energy intake, BMI, menopause, hormone therapy, diuretic use, hypertension, alcohol, vitamin C, caffeine, percentage of energy from carbohydrates

*Agency funding is that from government, university or not-for-profit health agency sources.
BMI, body mass index.

Study, year [Reference]	Participants	Cases	Weight	Risk Ratio [95% CI]
Choi *et al*, 2008 – Males [38]	46,393	775	50.6%	1.81 [1.31, 2.50]
Choi *et al*, 2010 – Females [39]	78,906	778	49.4%	1.44 [1.04, 2.00]
Total			100%	1.62 [1.28, 2.03]

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.95$; df = 1 (p=0.33); $I^2 = 0\%$
Overall association: Z = 4.10 (p < 0.0001)

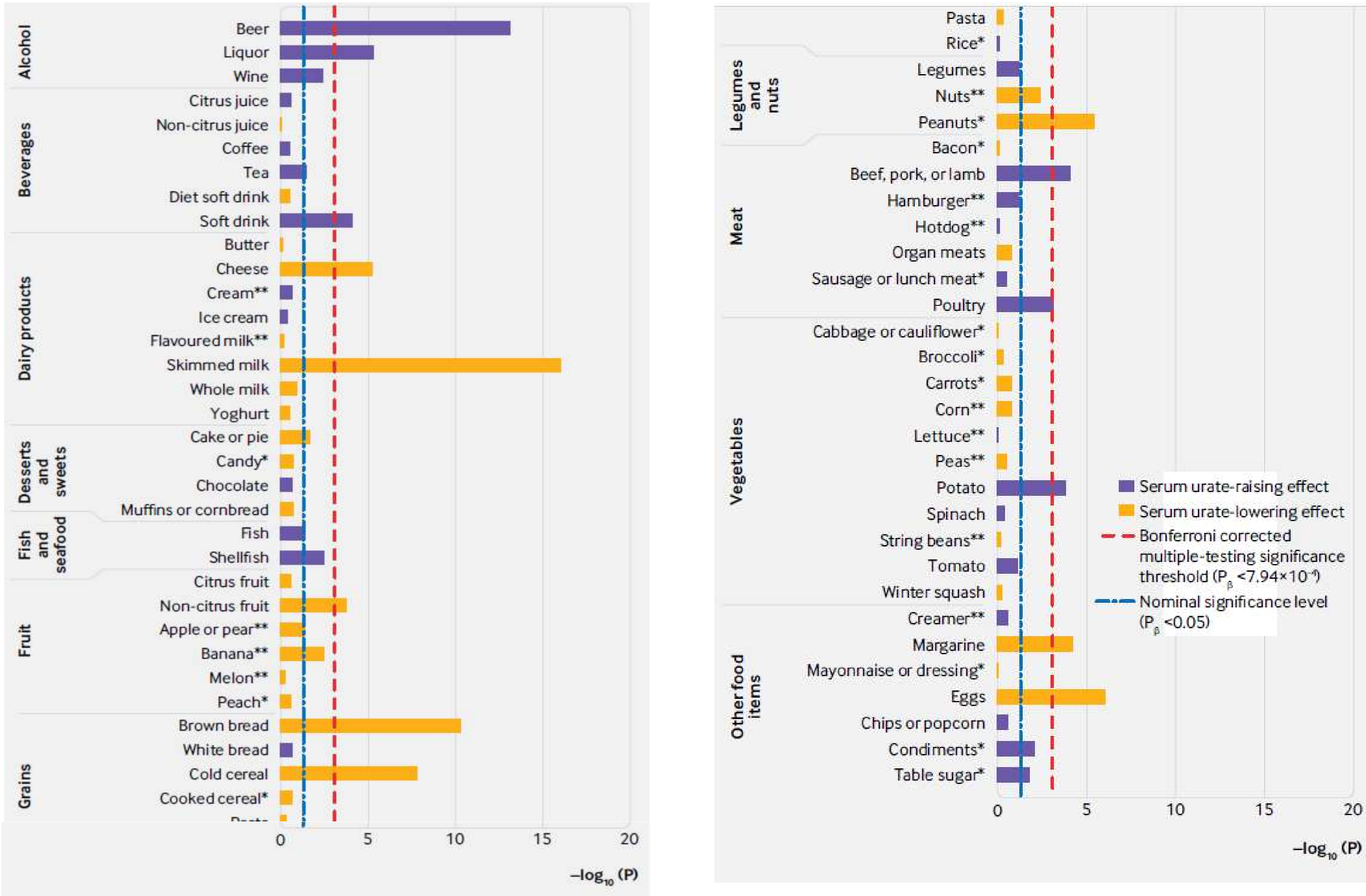
Risk ratio [95% CI]



Evaluation of the diet wide contribution to serum urate levels: meta-analysis of population based cohorts

BMJ 2017

Tanya J Major,[1] Ruth K Topless,[1] Nicola Dalbeth,[2] Tony R Merriman[1]



1 unité bière, alcools forts/jour : ↑ 9.7 µmol/L d'uricémie

Evaluation of the diet wide contribution to serum urate levels: meta-analysis of population based cohorts

BMJ 2017

Tanya J Major,[1] Ruth K Topless,[1] Nicola Dalbeth,[2] Tony R Merriman[1]

Table 1 | Diet wide significant associations with serum urate levels (μmol/L) in full, male, and female study cohorts

	Full cohort					Male cohort				Female cohort			
Food items	No	β (95% CI)†	P_β	R^2 (%)‡	β§	No	β (95% CI)	P_β	R^2 (%)	No	β (95% CI)	P_β	R^2 (%)
Associated with higher urate levels													
Beer	16 724	1.38 (1.02 to 1.74)¶	<0.001	0.99	3.91	8392	1.33 (0.93 to 1.74)¶	<0.001	1.31	8332	1.78 (1.22 to 2.34)	<0.001	0.49
Liquor	16 743	1.38 (0.79 to 1.98)¶	<0.001	0.40	2.46	8403	1.16 (0.46 to 1.86)¶	0.001	0.41	8340	1.84 (1.21 to 2.48)	<0.001	0.44
Wine	16 743	1.07 (0.34 to 1.80)¶	0.004	0.17	NA	8402	1.30 (0.64 to 1.96)	<0.001	0.16	8341	0.89 (−0.17 to 1.94)¶	0.10	0.20
Potato	16 754	0.87 (0.42 to 1.32)	<0.001	0.11	NA	8411	0.90 (0.25 to 1.56)	0.007	0.09	8343	0.77 (0.15 to 1.40)	0.02	0.09
Poultry	16 740	0.70 (0.29 to 1.10)	<0.001	0.08	NA	8403	0.94 (0.33 to 1.56)	0.003	0.10	8337	0.50 (−0.02 to 1.02)	0.06	0.05
Soft drink	16 745	0.68 (0.34 to 1.02)¶	<0.001	0.30	0.89; 0.58; 0.56	8404	0.79 (0.53 to 1.04)	<0.001	0.39	8341	0.55 (0.09 to 1.01)¶	0.02	0.16
Beef, pork, or lamb	16 757	0.63 (0.32 to 0.95)	<0.001	0.08	1.95; 0.43	8412	0.72 (0.28 to 1.16)	0.001	0.12	8345	0.47 (0.02 to 0.92)	0.04	0.04
Associated with lower urate levels													
Eggs	16 736	−1.10 (−1.54 to −0.66)	<0.001	0.13	NA	8403	−1.45 (−2.03 to −0.86)	<0.001	0.27	8333	−0.45 (−1.74 to 0.84)¶	0.49	0.01
Peanuts*	12 504	−0.88 (−1.25 to −0.51)	<0.001	0.18	NA	6277	−1.01 (−1.51 to −0.52)	<0.001	0.24	6227	−0.65 (−1.23 to −0.07)	0.03	0.07
Cold cereal	16 751	−0.72 (−0.97 to −0.47)	<0.001	0.14	NA	8409	−0.73 (−1.07 to −0.38)	<0.001	0.19	8342	−0.67 (−1.04 to −0.30)	<0.001	0.08
Skim milk	16 714	−0.63 (−0.78 to −0.48)	<0.001	0.40	−0.63	8390	−0.78 (−1.00 to −0.56)	<0.001	0.55	8324	−0.48 (−0.68 to −0.28)	<0.001	0.24
Cheese	16 755	−0.62 (−0.89 to −0.35)	<0.001	0.09	NA	8410	−0.64 (−1.05 to −0.23)	0.002	0.10	8345	−0.64 (−0.99 to −0.29)	<0.001	0.09
Brown bread	16 710	−0.60 (−0.77 to −0.42)	<0.001	0.22	NA	8382	−0.68 (−0.93 to−0.44)¶	<0.001	0.34	8328	−0.45 (−0.71 to −0.20)	<0.001	0.11
Margarine	16 716	−0.29 (−0.44 to −0.15)	<0.001	0.10	NA	8383	−0.25 (−0.69 to 0.18)¶	0.26	0.10	8333	−0.34 (−0.53 to −0.14)	<0.001	0.11
Non-citrus fruit	16 760	−0.28 (−0.43 to −0.13)	<0.001	0.06	NA	8414	−0.43 (−0.66 to −0.19)	<0.001	0.14	8346	−0.14 (−0.33 to 0.04)	0.13	0.01

NA=not applicable.
*Not all datasets were included in the analysis. The number of asterisks represents the number of datasets missing.
†Effect size, reflecting the change in serum urate level (μmol/L) per weekly serve.
‡Partial R^2 value (R^2_β) converted to a percentage (R^2×100) that quantitates the percent variance in serum urate levels explained by the food item.
§Values from significantly associated analyses from published data in combined men and women: beer and liquor were obtained from reference 21; soft drink data from references 18, 51, and 52; meat (beef, pork, or lamb) data from references 19 and 52; skim milk data from reference 52. References 18, 19, and 21 analysed NHANES III and therefore are not independent of our study.
¶A random effect model was used in the meta-analysis (P_{het}<0.1)

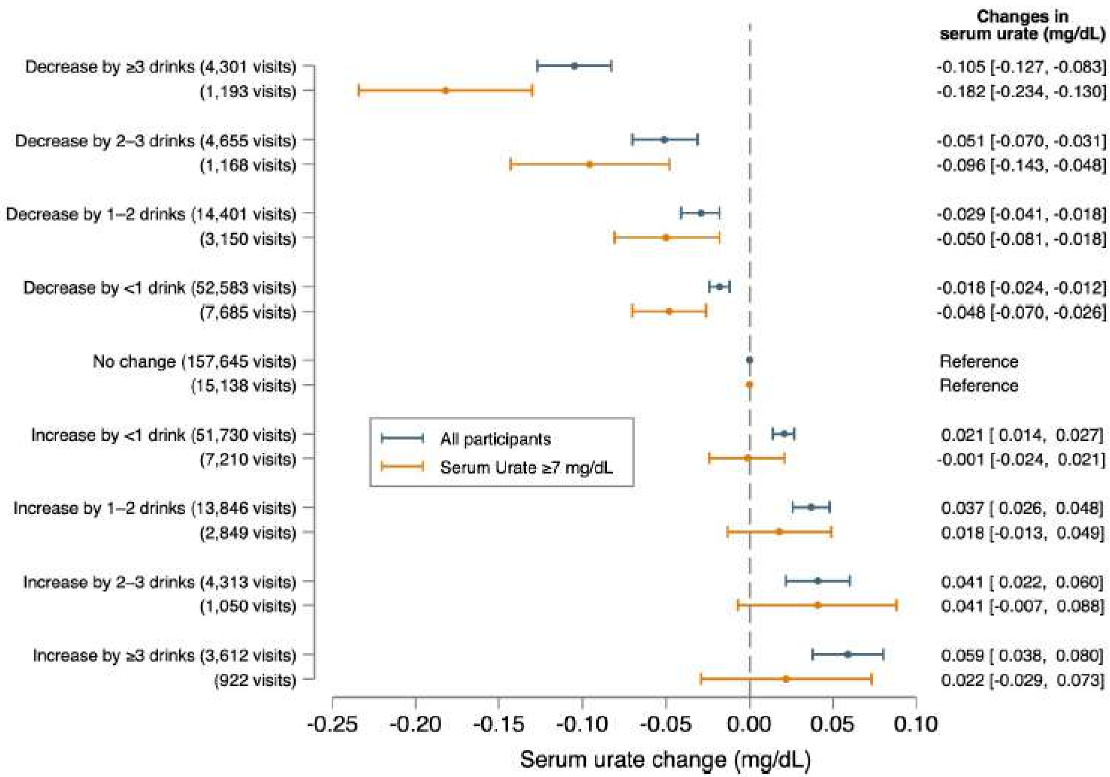
Facteurs alimentaires expliquent entre 0.06 à 0.99% l'uricémie

Les 14 aliments expliquent 3.3% et les 63 aliments évalués 4.3 %

EPIDEMIOLOGICAL SCIENCE

Changes in alcohol intake and serum urate changes: longitudinal analyses of annual medical examination database

Fukui 2024 Ann Rheum Dis



Small impact on SUL with alcohol withdraw (-1.8 mg/L/U)

Effects of Dietary Patterns on Serum Urate: Results From a Randomized Trial of the Effects of Diet on Hypertension

Arthritis Rheumatol 2021

Stephen P. Juraschek,[1] Chio Yokose,[2] Natalie McCormick,[2] Edgar R. Miller III,[3] Lawrence J. Appel,[3] and Hyon K. Choi[2]

Table 1. Baseline characteristics of the participants according to dietary assignment*

	Control (n = 107)	FV (n = 110)	DASH (combination) (n = 110)
Age, years	45.1 ± 11.7	46.3 ± 10.9	44.8 ± 10.5
Female, %	43.0	44.5	52.7
African American, %	49.5	48.2	53.6
Body mass index ≥30 kg/m^2, %	36.4	36.4	36.4
Body mass index, kg/m^2	28.0 ± 3.9	27.9 ± 4.0	28.3 ± 3.9
Hypertension, %	27.1	27.3	24.5
Systolic BP, mm Hg	130.7 ± 10.8	131.5 ± 11.3	130.9 ± 10.3
Diastolic BP, mm Hg	85.0 ± 4.5	84.3 ± 4.9	84.3 ± 4.4
LDL cholesterol, mg/dl†	121.8 ± 30.8	127.9 ± 30.6	117.1 ± 33.3

DASH = Dietary Approches to Stop Hypertension

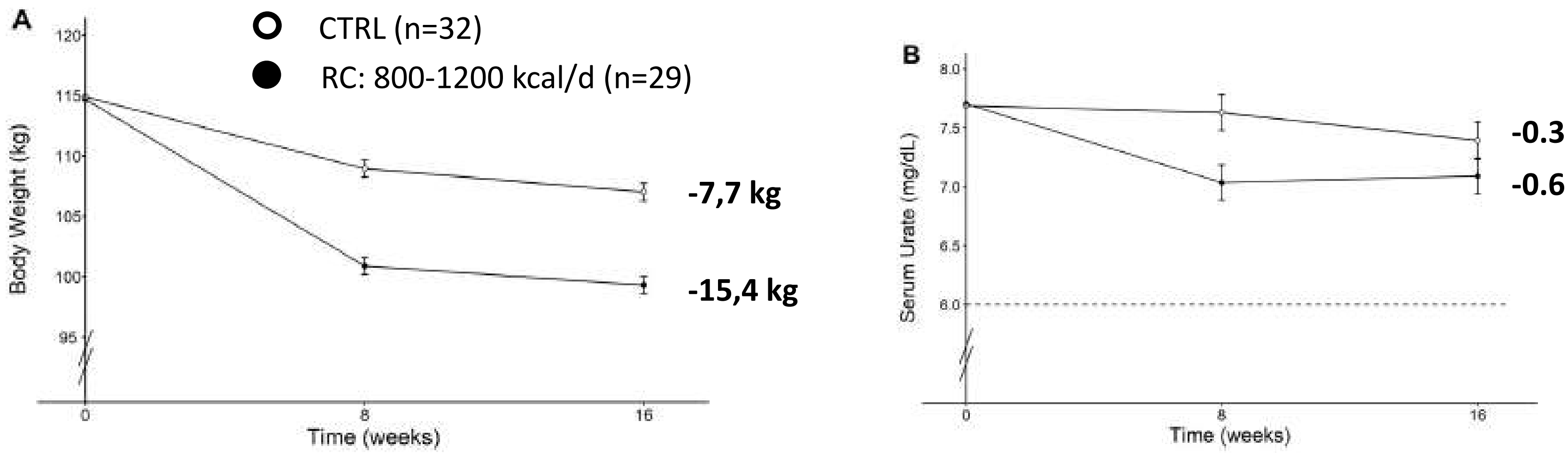
FV : fruits and vegetables

DASH: fat-free or low-fat dairy products
Restrict saturated fat, total fat, cholesterol, sweets, and sugar-containing beverage consumption

Weight Loss for Patients With Gout and Concomitant Obesity: A Proof-of-Concept Randomized Trial

Arthritis Rheumatol 2024

Robin Christensen,[1] Kristian Zobbe,[2] Sabrina M. Nielsen,[1] Lisa K. Stamp,[3] Marius Henriksen,[2] Anders F. Overgaard,[2] Lene Dreyer,[4] Filip K. Knop,[5] Jasvinder A. Singh,[6] Michael Doherty,[7] Pascal Richette,[8] Arne Astrup,[9] Karen Ellegaard,[2] Else M. Bartels,[10] Mikael Boesen,[2] Henrik Gudbergsen,[2] Henning Bliddal,[2] and Lars Erik Kristensen[2]



→ **Small impact on SUL with weight loss (- 4 mg/L/10 kg)**

EXTENDED REPORT

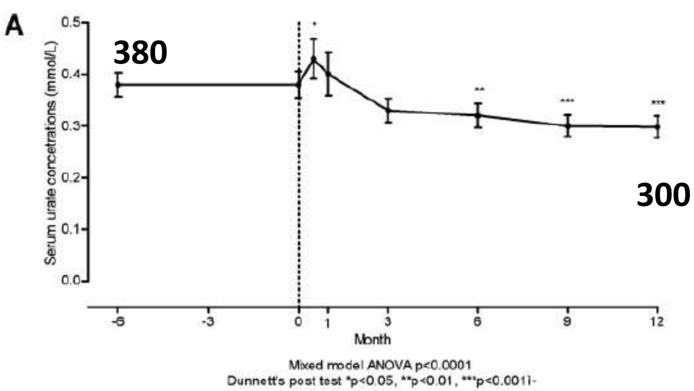
Impact of bariatric surgery on serum urate targets in people with morbid obesity and diabetes: a prospective longitudinal study

Nicola Dalbeth,[1,2] Peggy Chen,[1] Marie White,[3] Gregory D Gamble,[2] Caran Barratt-Boyes,[4] Peter J Gow,[1] Brandon Orr-Walker[4]

2013 Ann Rheum Dis

N=60, BMI 47.9 kg/m2

Weight loss over 12 months : -34,3 kg



-3.9 mg/L/10 kg

Weight Loss, Xanthine Oxidase, and Serum Urate Levels: A Prospective Longitudinal Study of Obese Patients

PASCAL RICHETTE,[1] CHRISTINE POITOU,[2] PHILIPPE MANIVET,[3] JÉROME DENIS,[3] JEAN-LUC BOUILLOT,[4] KARINE CLÉMENT,[2] JEAN-MICHEL OPPERT,[2] AND THOMAS BARDIN[1]

Arthritis Ther Res 2016

N=156, BMI 47.8 kg/m2

	Baseline	6 months	Absolute change	p
Weight (Kg)	131.8 ±23.8	100.5 ± 19.9	31.3 ± 7.8	
SUL (mg/L)	55.2 ± 13.3	49.8 ± 12.1	5.4 ±10.6	0.001
XO activity	42.5 ± 12.3	34.8 ± 7.0	7.4 ± 12.1	<0.001

-1.7 mg/L/10 kg

→ Small impact on SUL with weight loss

Effects of Dietary Patterns on Serum Urate: Results From a Randomized Trial of the Effects of Diet on Hypertension

Stephen P. Juraschek,[1] Chio Yokose,[2] Natalie McCormick,[2] Edgar R. Miller III,[3] Lawrence J. Appel,[3] and Hyon K. Choi[2]

Arthritis Rheumatol 2021

Table 2. Serum urate levels in participants assigned to each diet*

Diet	Baseline, mg/dl	8 weeks, mg/dl	Difference (95% CI)	*P*
Control (n = 107)	5.65 ± 1.56	5.68 ± 1.55	0.03 (−0.10, 0.16)	0.67
FV (n = 110)	5.85 ± 1.27	5.68 ± 1.27	−0.17 (−0.28, −0.06)	0.004
DASH (n = 110)	5.59 ± 1.55	5.37 ± 1.42	−0.22 (−0.35, −0.08)	0.002

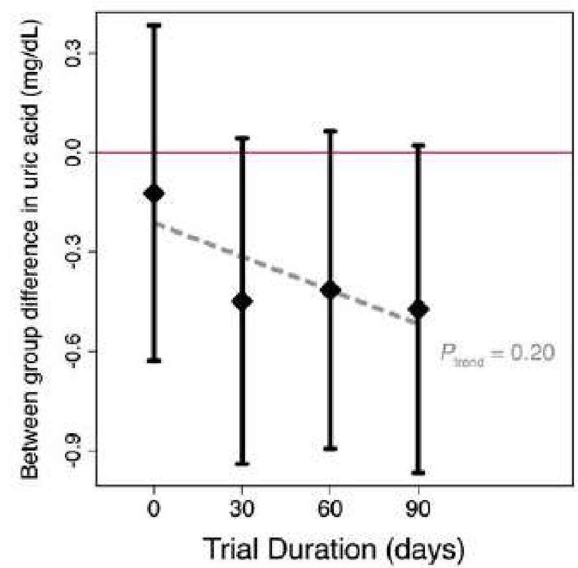
* Except where indicated otherwise, values are the mean ± SD. 95% CI = 95% confidence interval (see Table 1 for other definitions).

DASH diet decreases SUL (-2.2 mg/L) after 1 month

DASH Diet and Change in Serum Uric Acid over Time

Olive Tang, AB[1], Edgar R Miller III, MD, PhD[1,2], Allan C Gelber, MD, PhD[1,2], Hyon K Choi, MD, DrPH[3], Lawrence J Appel, MD, MPH[1,2], and Stephen P Juraschek, MD, PhD[1,2]

Clin Rheumatol 2017



Evaluation of the diet wide contribution to serum urate levels: meta-analysis of population based cohorts

BMJ 2017

Tanya J Major,[1] Ruth K Topless,[1] Nicola Dalbeth,[2] Tony R Merriman[1]

Table 2 | Percent variance in serum urate levels (μmol/L) explained by dietary and genetic factors in full, male, and female study cohorts

Diet, genetic score, and additional adjuster	Full cohort				Male cohort				Female cohort			
	No	β (95% CI)*	P_β	R^2 (%)†	No	β (95% CI)	P_β	R^2 (%)	No	β (95% CI)	P_β	R^2 (%)
Genetic effect												
Genetic risk score												
Unadjusted	12 162	0.99 (0.93 to 1.05)	<0.001	7.85	6109	0.93 (0.84 to 1.03)	<0.001	5.89	6053	1.04 (0.97 to 1.12)	<0.001	10.55
Healthy Eating	12 162	0.99 (0.93 to 1.05)	<0.001	7.82	6109	0.93 (0.84 to 1.03)	<0.001	5.87	6053	1.04 (0.96 to 1.12)	<0.001	10.51
DASH	12 147	0.99 (0.93 to 1.05)	<0.001	7.85	6106	0.94 (0.84 to 1.03)	<0.001	5.91	6041	1.04 (0.96 to 1.12)	<0.001	10.55
Mediterranean	12 131	0.99 (0.93 to 1.05)	<0.001	7.86	6092	0.94 (0.84 to 1.03)	<0.001	5.93	6039	1.04 (0.97 to 1.12)	<0.001	10.53
Data driven	12 078	0.99 (0.93 to 1.05)	<0.001	7.84	6063	0.94 (0.84 to 1.03)	<0.001	5.89	6015	1.04 (0.97 to 1.12)	<0.001	10.53
Heritability estimate												
Unadjusted	12 162	NA	<0.001	23.9 (20.2 to 27.5)	6109	NA	<0.001	23.8 (16.6 to 30.0)	6053	NA	<0.001	40.3 (33.5 to 47.1)

NHANES III was unable to be included in the genetic risk score or heritability analyses

L'héritabilité explique 23.8 (hommes) à 40.3% (femmes) de la variance de l'uricémie

Heritability of Clinical Chemistries in an Older Twin Cohort: The NHLBI Twin Study

Genetic Epi 1987

Sona Kalousdian, Richard Fabsitz, Richard Havlik, Joe Christian, and Ray Rosenman

TABLE IV. Comparisions of Heritabiility Estimates From Three Studies

Test	Brazil	Australia	NHLBI Exam 1	NHLBI Exam 2
Albumin	0.773	0.73	—	0.36
Alkaline phosphatase	0.813	0.71[a]	—	0.59
Bilirubin	0.787	0.71	0.48	NS
Blood urea nitrogen	0.546	NS	0.56	0.48
Glucose	0.734	—	0.88	0.52
Phosphorus	0.588	0.54	—	0.54
Total protein	0.733	0.62	—	0.53
Uric acid	0.680	0.73	0.52	0.45

NS, clinical chemistry was analyzed, but result was not significantly different from zero; —, clinical chemistry was not tested or analysis was not done because of significantly different means or common environment by zygosity.

[a]Estimate is for males aged 19–34 years and does not include female twins (in contrast to the other Australian results).

Héritabilité de l'uricémie expliquée par les SNP communs : 27-41% (Kottgen 2013 Nat Genet).

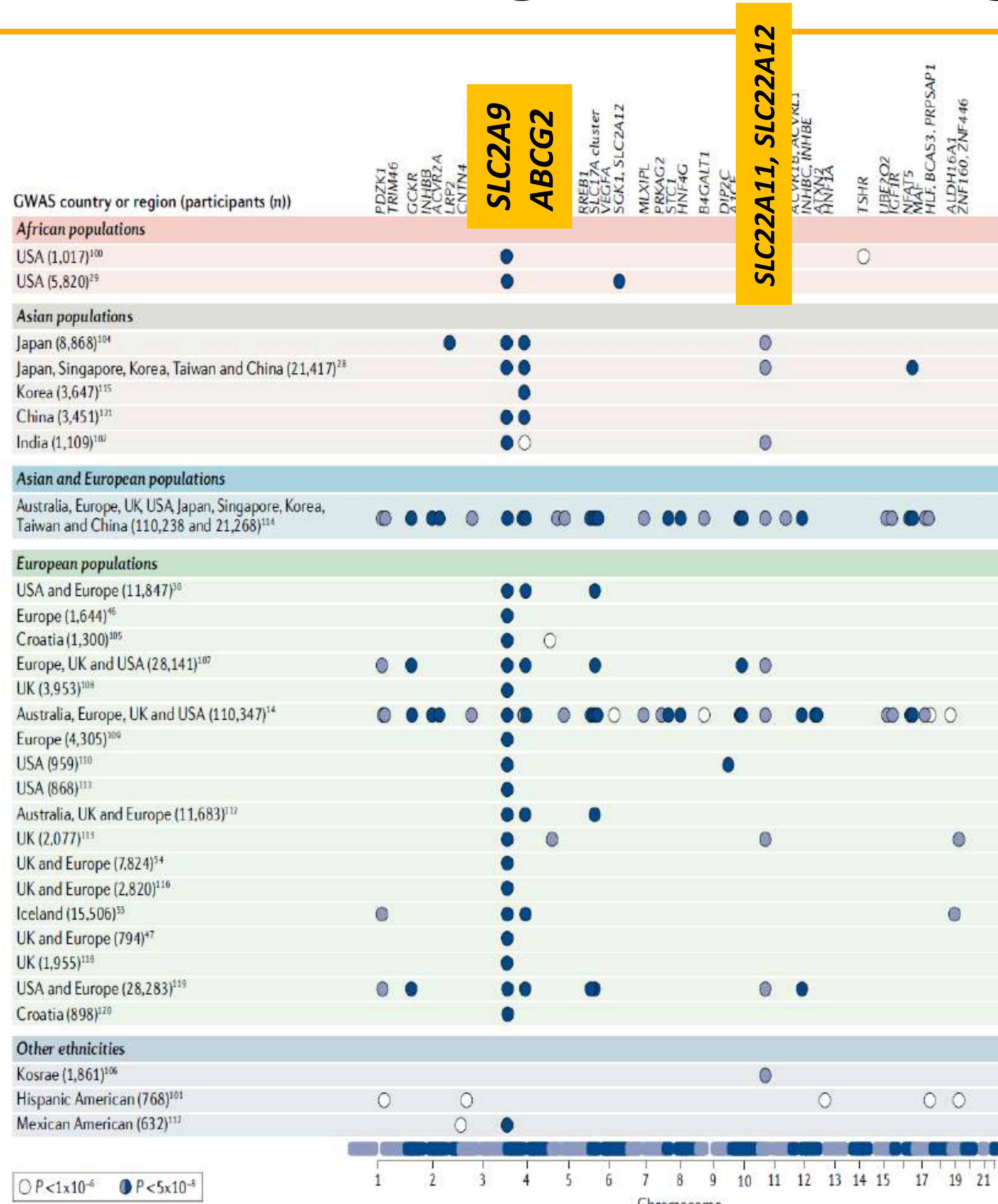
Uricémie: une régulation multigénique

Études d'association pangénomique (GWAS)

> 80 gènes associés au taux sérique de l'urate (AU)

Transporteurs de l'urate

(rein>>>intestin)



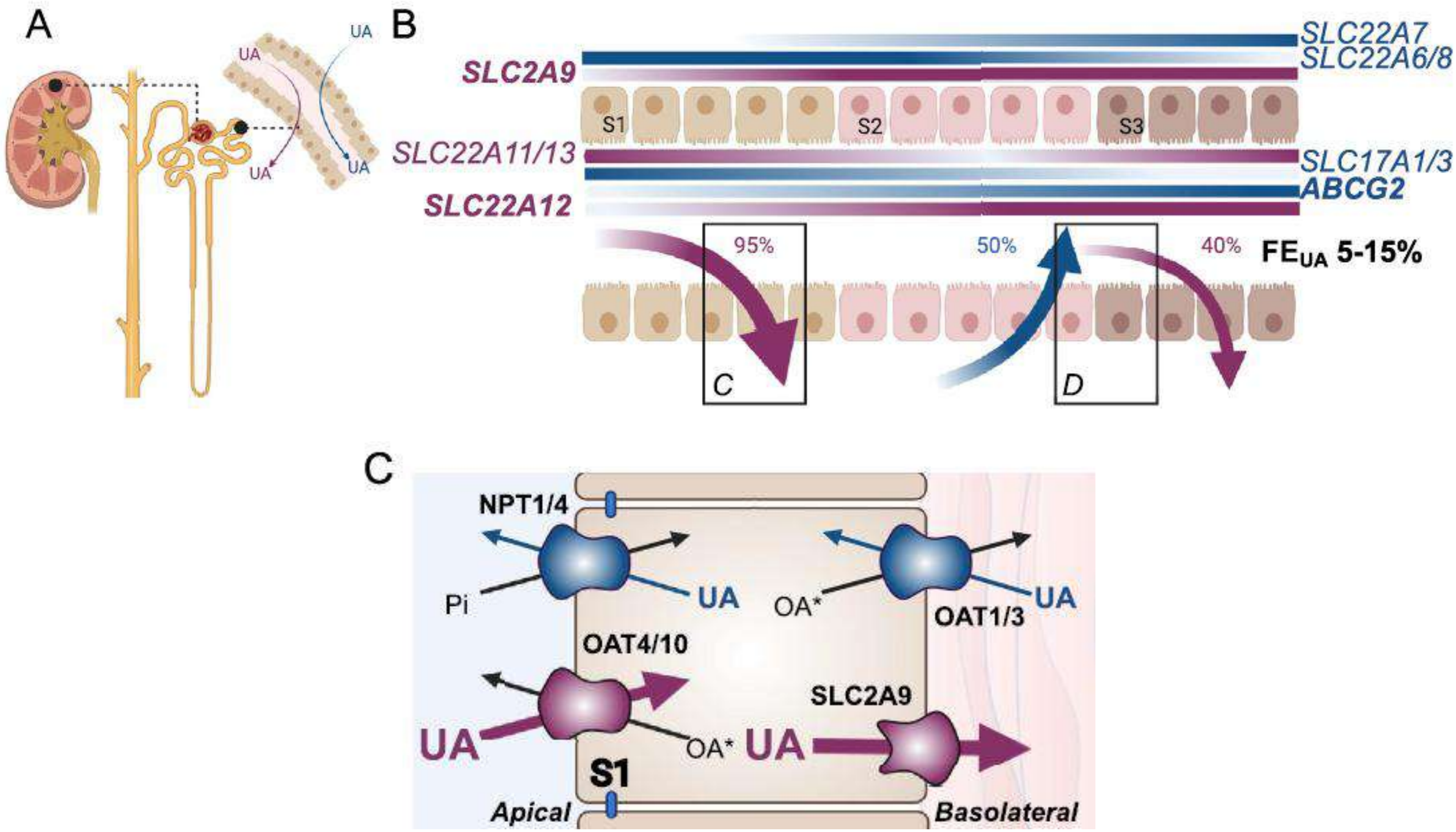
GWAS uricémie

SLC2A9 (GLUT9*)*: Presque toutes les populations

SLC22A12 (URAT1*)*
ABCG2 (ATP binding cassette subfamily G member 2) : Nombreuses populations

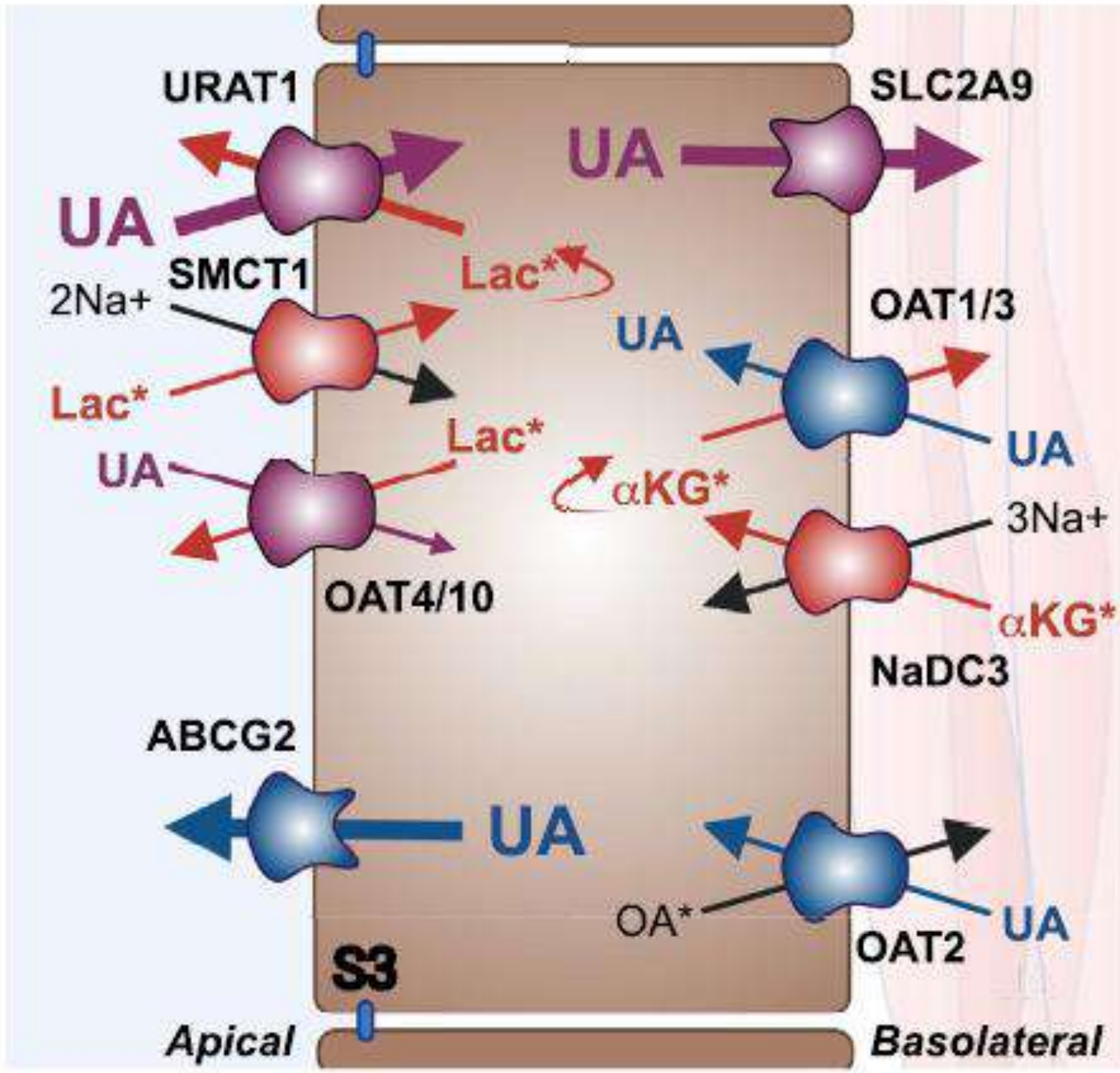
Major T 2018 Nat Rev Rheum

Uricémie: régulation rénale



Halperin Kuhns 2021 BPRCR

Uricémie: régulation rénale

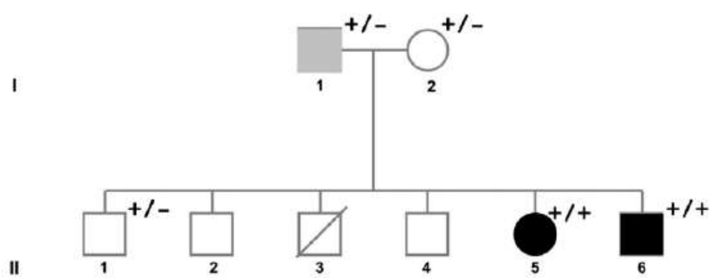


Halperin Kuhns 2021 BPRCR

Early-onset gout and rare deficient variants of the lactate dehydrogenase D gene

Rheumatology 2023

Thomas Bardin[1,2,*], Yves-Marie Ducrot[3], Quang Nguyen[2], Emmanuel Letavernier[4], Jeremy Zaworski[4], Hang-Korng Ea[1], Fréderic Touzain[5], Minh Duc Do[6], Julien Colot[7], Yann Barguil[7], Antoine Biron[7], Matthieu Resche-Rigon[8], Pascal Richette[1], Corinne Collet[1]



II-6 : goutte à 9 ans. Polyarticulaires, inflammation chroniques, tophi, destruction articulaire. Uricémie 581 µmol/L, DFG 112 ml/min/1,73m2

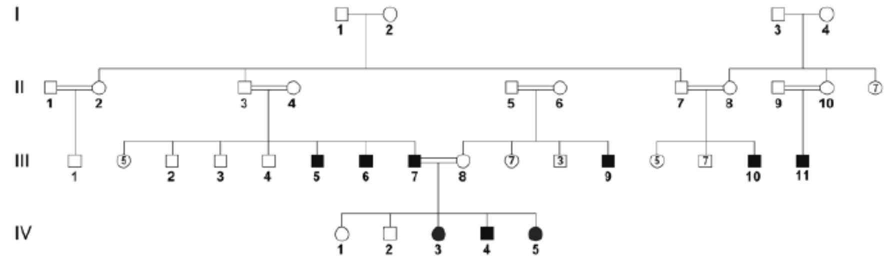
II-5: cas index, femme goutte à 21 ans. Polyarticulaire, tophus et arthropathies. Uricémie 545 µmol/L, DFG 69 ml/min/1,73m2

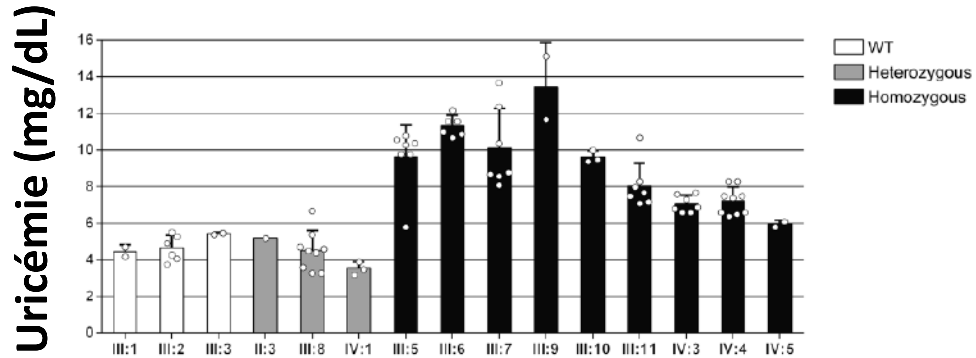
Mutations non fonctionnelles de *LDH-D*

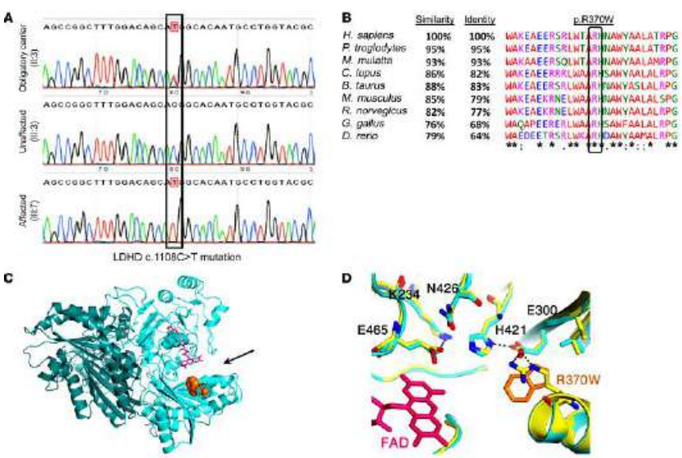
JCI The Journal of Clinical Investigation **2020**

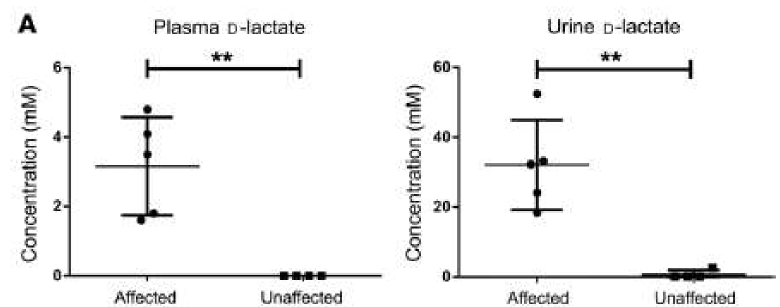
Hyperuricemia and gout caused by missense mutation in d-lactate dehydrogenase

Max Drabkin, ... , Yonatan Perez, Ohad S. Birk





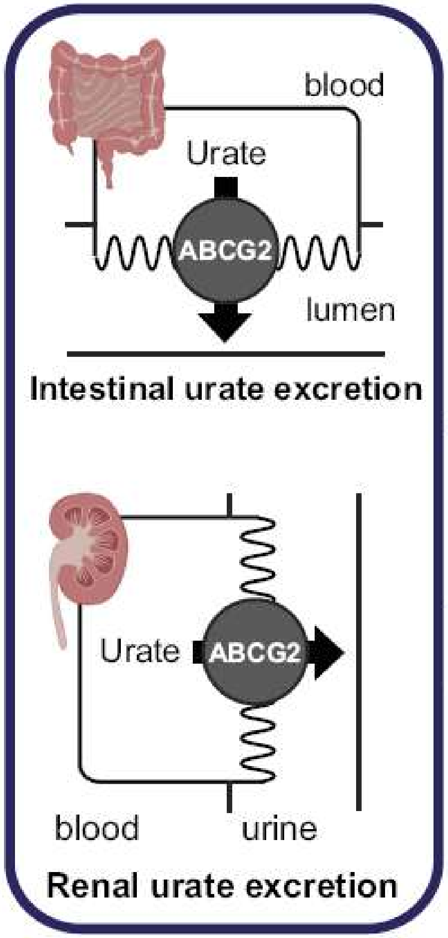




Accumulation de D-lactate favorise la réabsorption de l'acide urique via URAT1, responsable de l'hyperuricémie et de la goutte

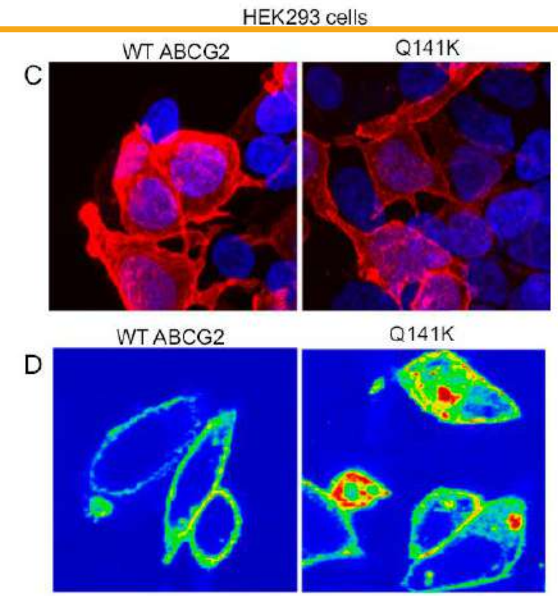
ABCG2 et goutte

- Excrète les médicaments des cellules
- Excrète l'urate des cellules tubulaire rénales et des *entérocytes*
- Explique un certain nombre de gouttes juvéniles
- Au japon, les variants conduisant à une diminution d'activité d'ABCG2, favorisent la goutte par diminution de l'excrétion rénale et intestinale d'urate



Matsuo 2014 Sci Report

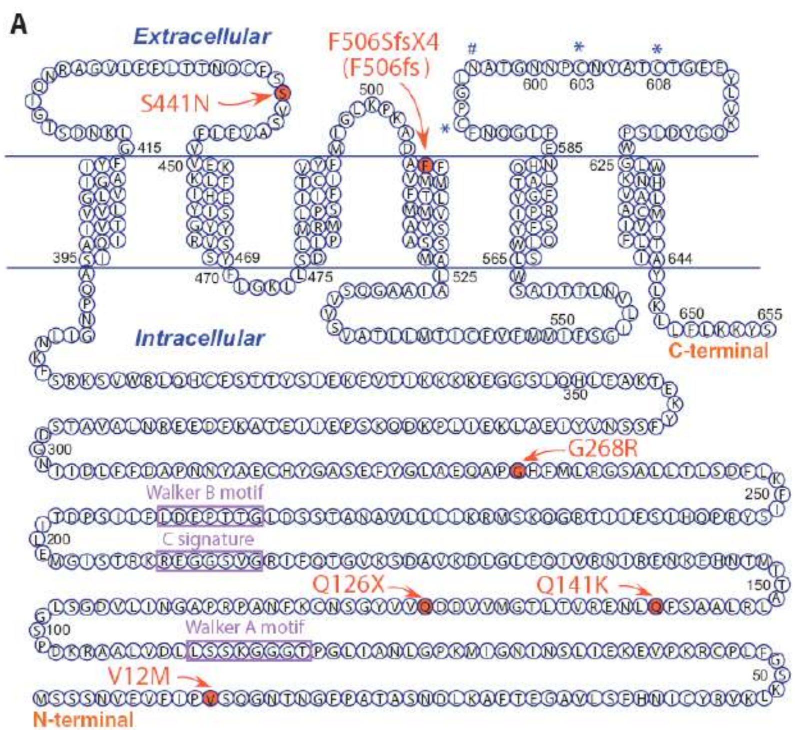
Variants du gène ABCG2

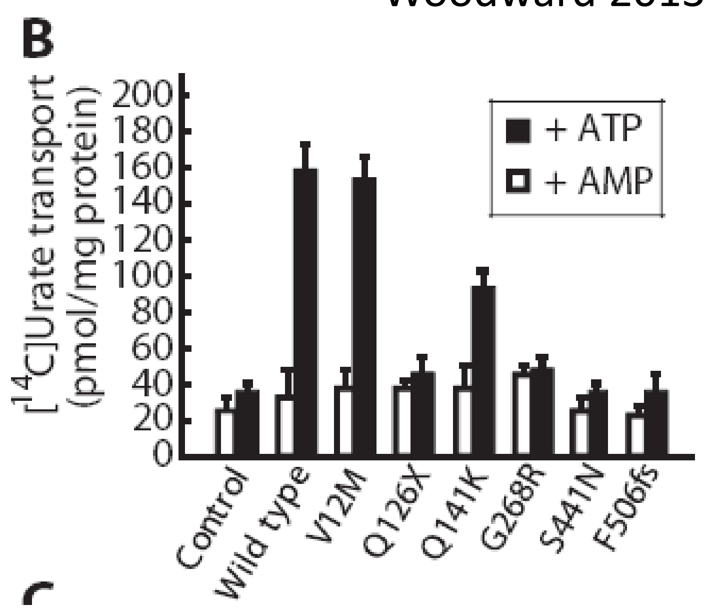


Q126X = variant non fonctionnel

Q141K = variant avec perte de 54% de la fonction

Woodward 2013 PNAS





Matsuo 2009 Sci Translat Med

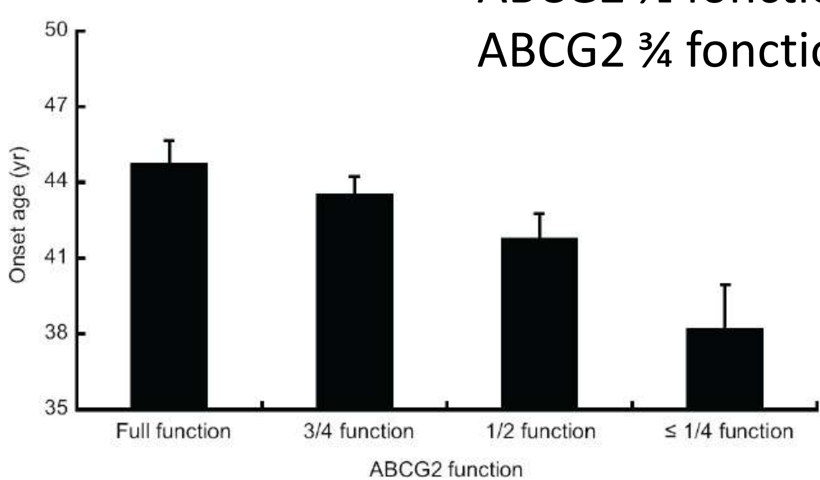
Variants ABCG2 et goutte

Table 1 | ABCG2 functions of participants

	Genotype Combination		Number (%)	
Estimated Function	Q126X* (rs72552713)	Q141K* (rs2231142)	Gout	Control
≤1/4 function	**T**/**T**	C/C	37 (5.2)	22 (1.2)
	T/C	C/**A**		
1/2 function	**T**/C	C/C	169 (24.0)	219 (11.6)
	C/C	**A**/**A**		
3/4 function	C/C	C/**A**	331 (47.0)	699 (37.0)
Full function	C/C	C/C	168 (23.8)	947 (50.2)
Total			705 (100.0)	1,887 (100.0)

*Risk alleles (T for Q126X, A for Q141K) are indicated in bold type at four locations, respectively.

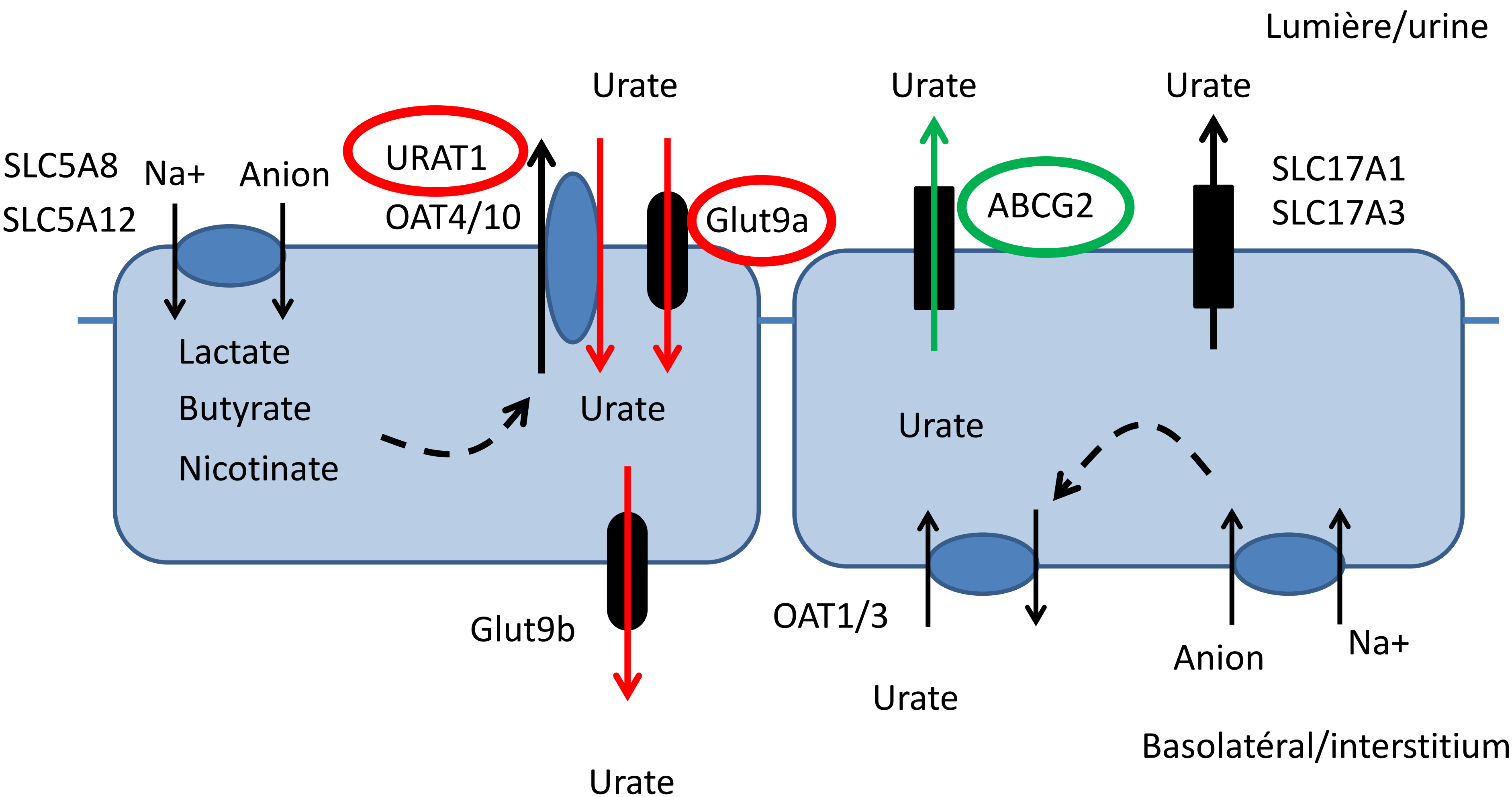
ABCG2 ¼ fonction: RR goutte juvénile 22.2 (IC95 5.89-83.7)
ABCG2 ½ fonction: RR goutte juvénile 15.3 (IC95 7.53-30.9)
ABCG2 ¾ fonction: RR goutte juvénile 6.47 (IC95 3.31-12.7)



Goutte juvénile : début avant 20 ans

Matsuo 2013 Sci Report

Uricémie: régulation rénale

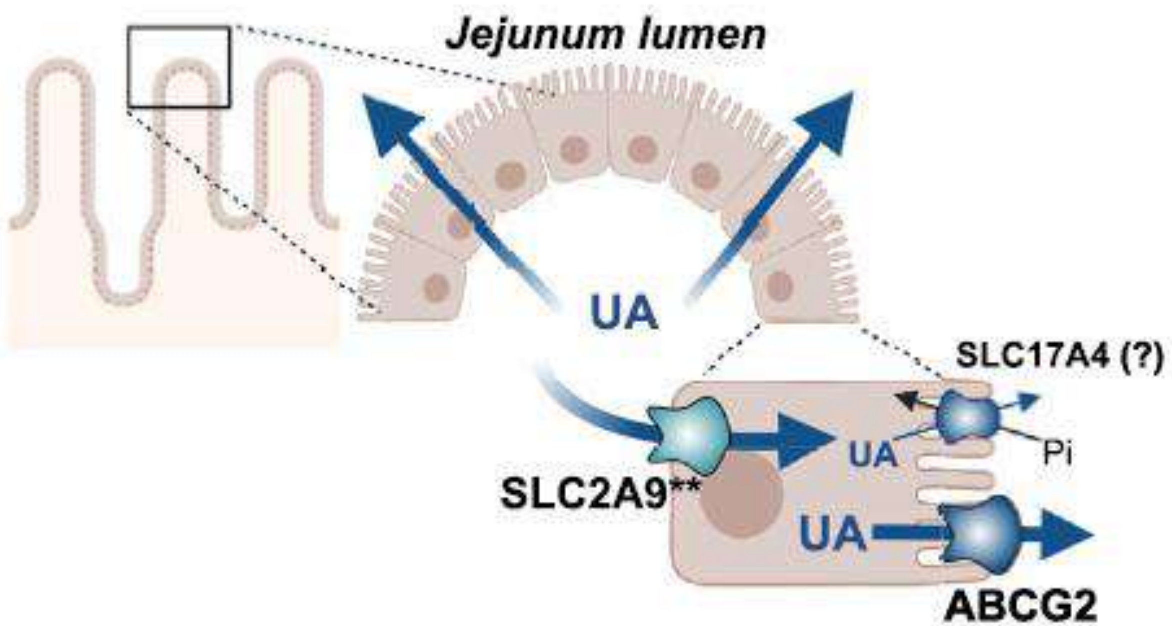


Uricémie: régulation digestive

Table 1. Uric acid transporters in the intestine.

Name	Encoding gene	Studying stage	References
ABCG2/BCRP	*ABCG2*	*In vitro, in vivo,* in clinic	Sarkadi et al. (2004), Nakayama et al. (2011), Hosomi et al. (2012), Ichida et al. (2012), Matsuo et al. (2014), Takada et al. (2014) and Yano et al. (2014)
MRP2	*ABCC2*	*In vivo*	Dudas et al. (2005), Hilgendorf et al. (2007) and Grandvuinet et al. (2012)
MRP4	*ABCC4*	*In vivo*	Dudas et al. (2005), Hilgendorf et al. (2007) and Grandvuinet et al. (2012)
GLUT9	*SLC2A9*	*In vivo*	Phay et al. (2000) and, DeBosch et al. (2014)
MCT9	*SLC16A9*	In clinic	Nakayama et al. (2013)
NPT4	*SLC17A3*	No study	Reimer and Edwards (2004)
NPT homolog (NPT5)	*SLC17A4*	*In vivo*	Shibui et al. (1999) and Togawa et al. (2012)
OAT10	*SLC22A13*	*In vitro, in vivo*	Bahn et al. (2008)
YgfU	*ygfU*	*In vitro*	Papakostas and Frillingos (2012)

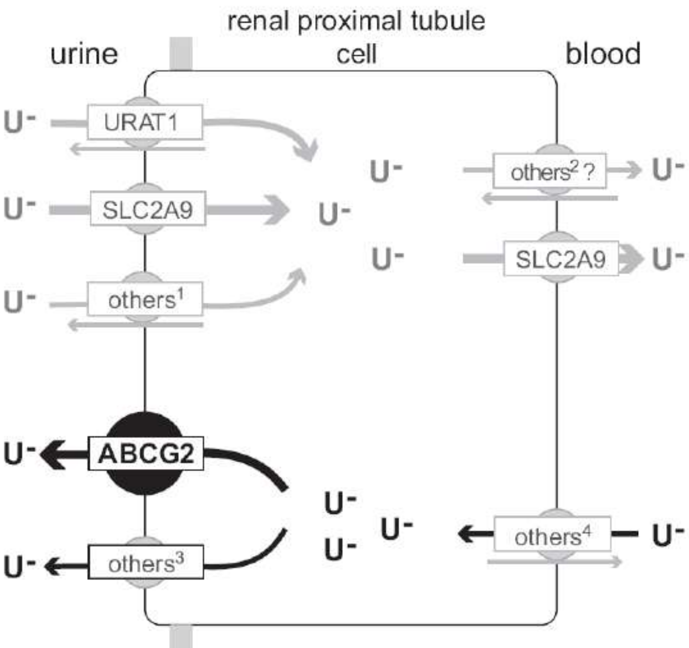
Xu 2016 Pharmaceutical Biol

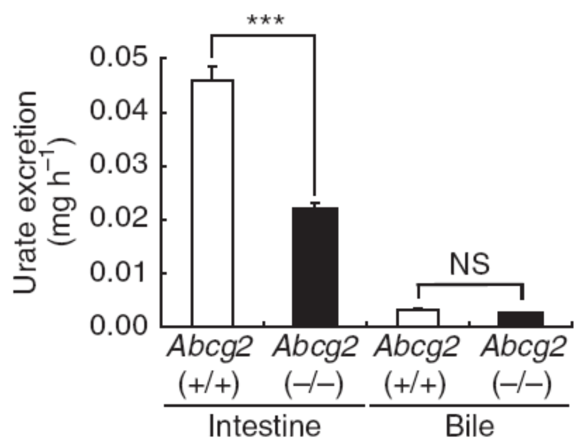


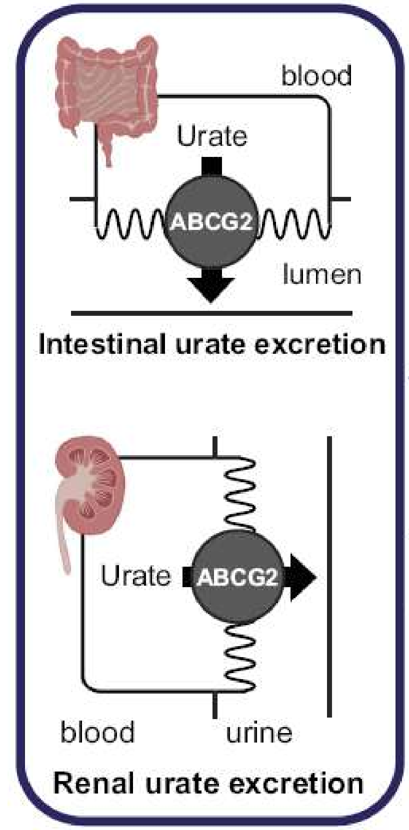
Halperin Kuhns 2021 BPRCR

ABCG2: excrétion digestive de l'urate

ABCG2 est exprimé par de nombreux tissus





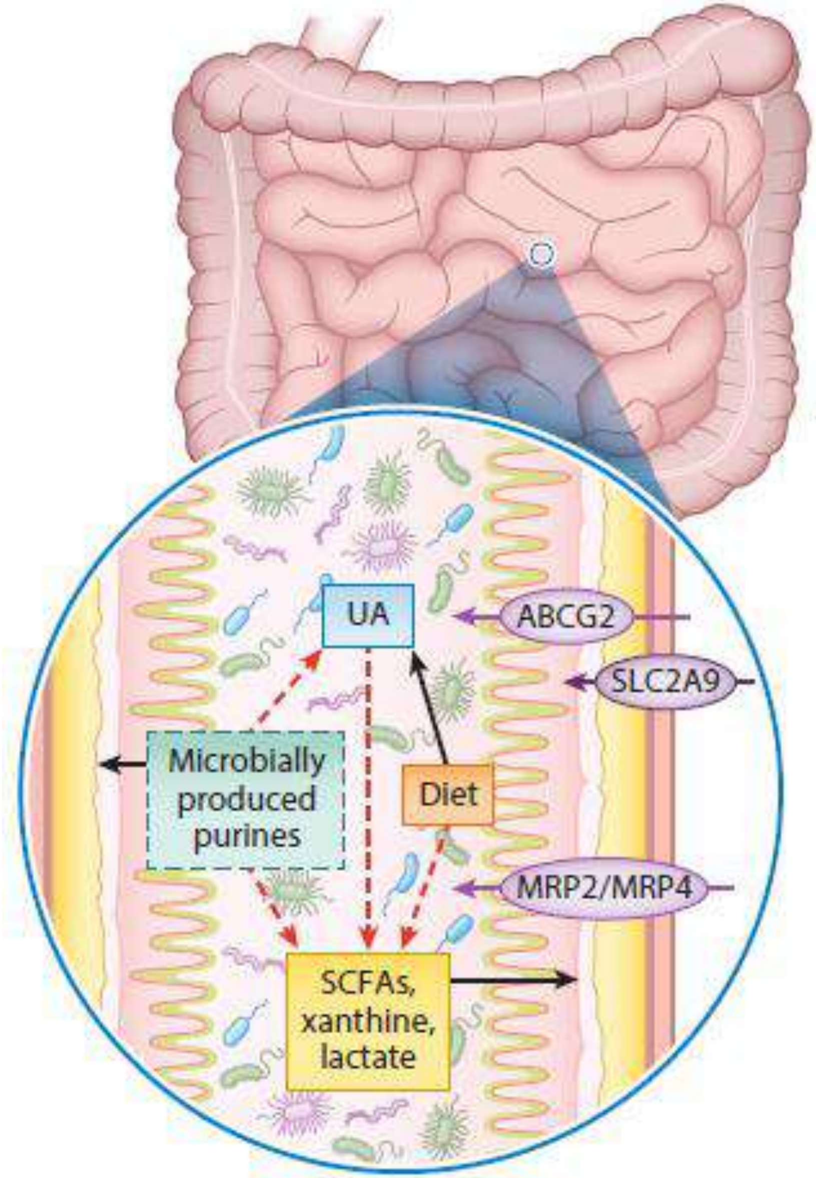


ABCG2 (*ATP-Binding Cassette, subfamily G*) = BCRP (*Breast Cancer Resistance Protein*)

Woodward 2009 PNAS

Matsuo 2009 Sci Translat Med

Uricémie: régulation digestive

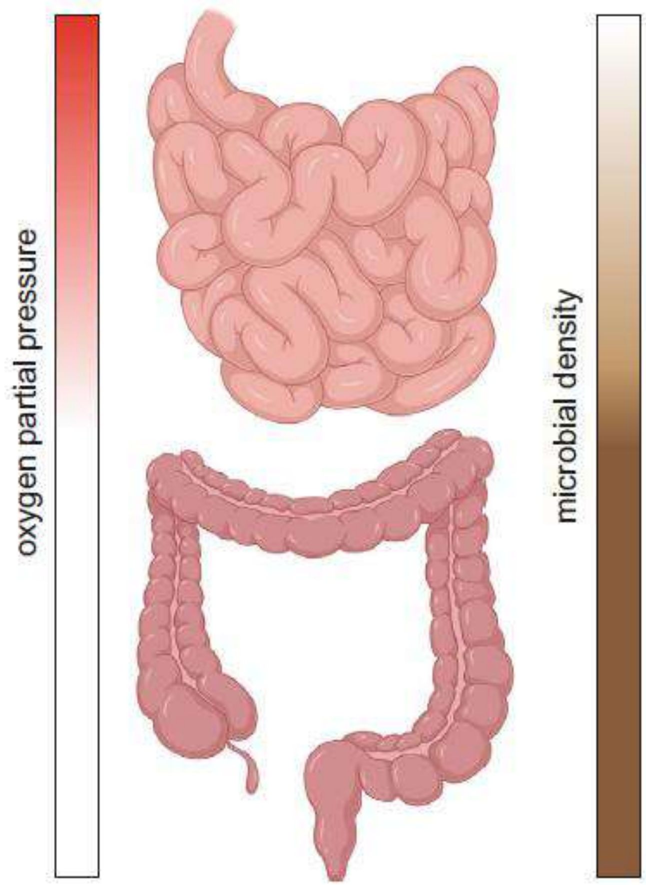


Et le microbiote…

Emery 2025 Ann Rev Microbio

The Gut Microbiome in Hyperuricemia and Gout

Robert Terkeltaub[1] and Dylan Dodd[2] *Arthritis Rheum 2025*



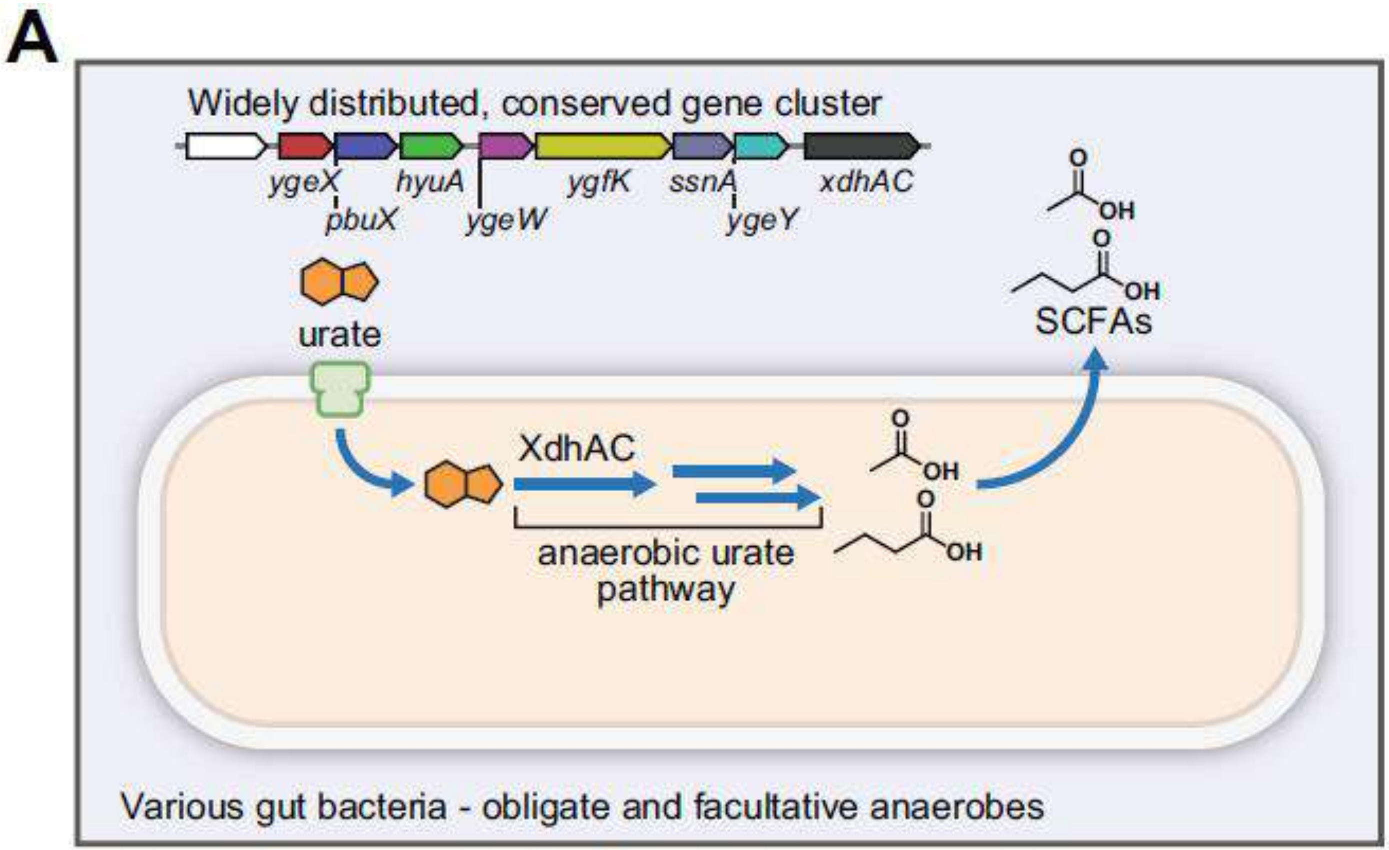
Principal small intestinal bacterial Phyla
(Mainly aerobic and facultative anaerobic bacteria)
Primarily Bacillota (e.g., Lactobacilli and Clostridia)
~30% of gut microbiome
Also: Bacteroidota, Pseudomonadota, Fusobacteriota, Actinomycetota
~$10^{4\text{-}5}$ CFU/mL in harsh duodenal environment
~$10^{7\text{-}8}$ CFU/mL in terminal ileum

Principal large intestinal bacterial Phyla
(Mainly obligate anaerobic bacteria)
Bacteroidota: ~30% of gut microbiome
Also: Pseudomonadota, Actinomycetota, Bacillota
~$10^{10\text{-}11}$ CFU/mL

Large intestine is deeply anaerobic
Low O_2 levels limit uricase activity in the distal small intestine and colon

The Gut Microbiome in Hyperuricemia and Gout

Robert Terkeltaub[1] and Dylan Dodd[2] *Arthritis Rheum 2025*

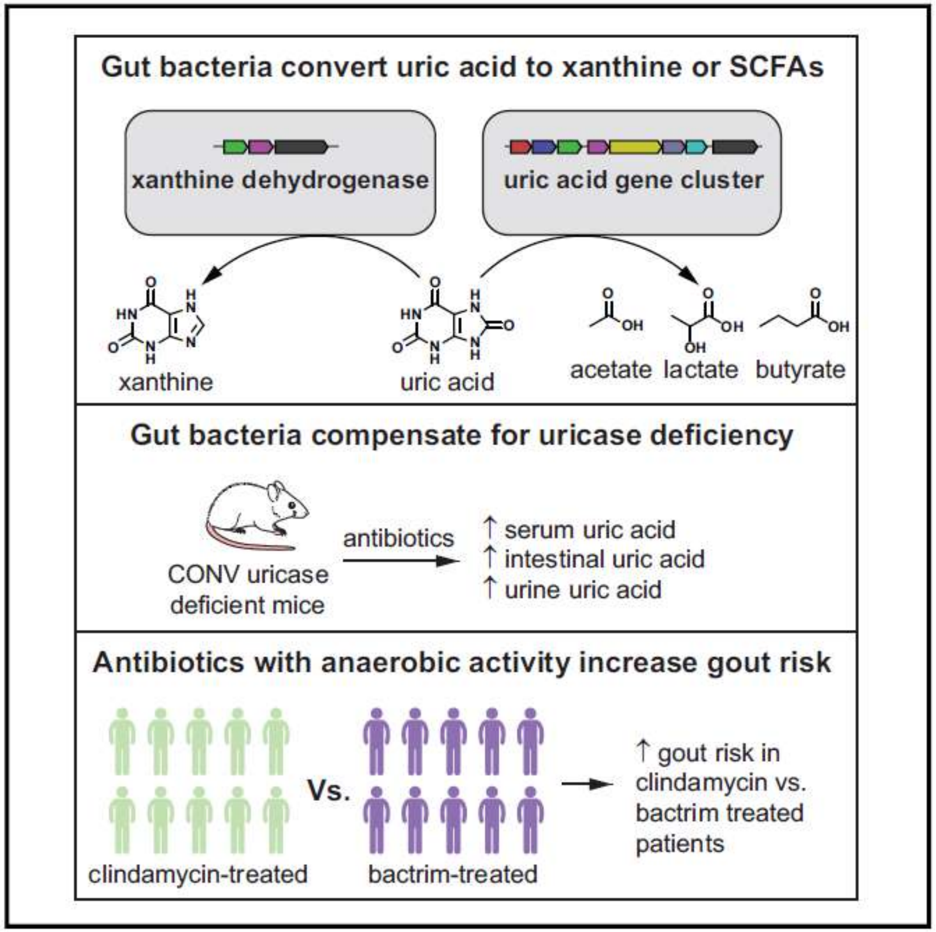


Cell 2023

Article

A widely distributed gene cluster compensates for uricase loss in hominids

Graphical abstract



Authors

Yuanyuan Liu, J. Bryce Jarman, Yen S. Low, ..., Alan C. Pao, Saurabh Gombar, Dylan Dodd

Correspondence

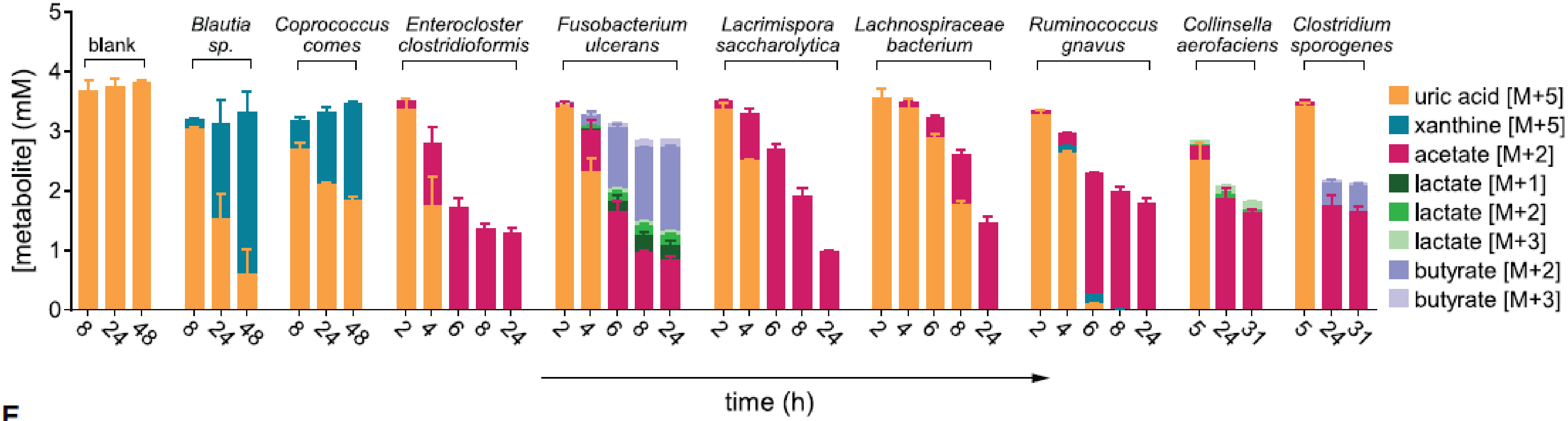
ddodd2@stanford.edu

In brief

Anaerobic bacteria of the gut microbiome are able to metabolize uric acid, compensating for the uricase deficiency of their host. This conversion of uric acid to xanthine or SCFAs is important for maintaining low levels of uric acid in serum, lowering gout risk.

Cell

A widely distributed gene cluster compensates for uricase loss in hominids



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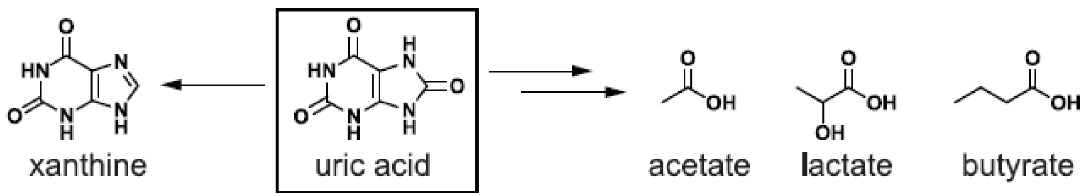


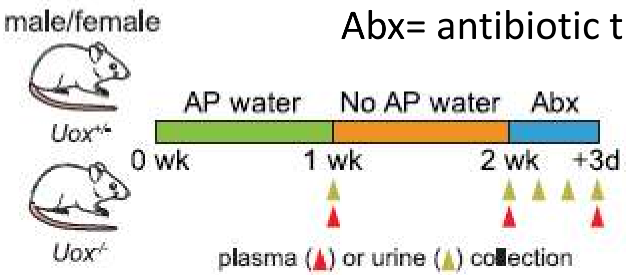
Liu 2023

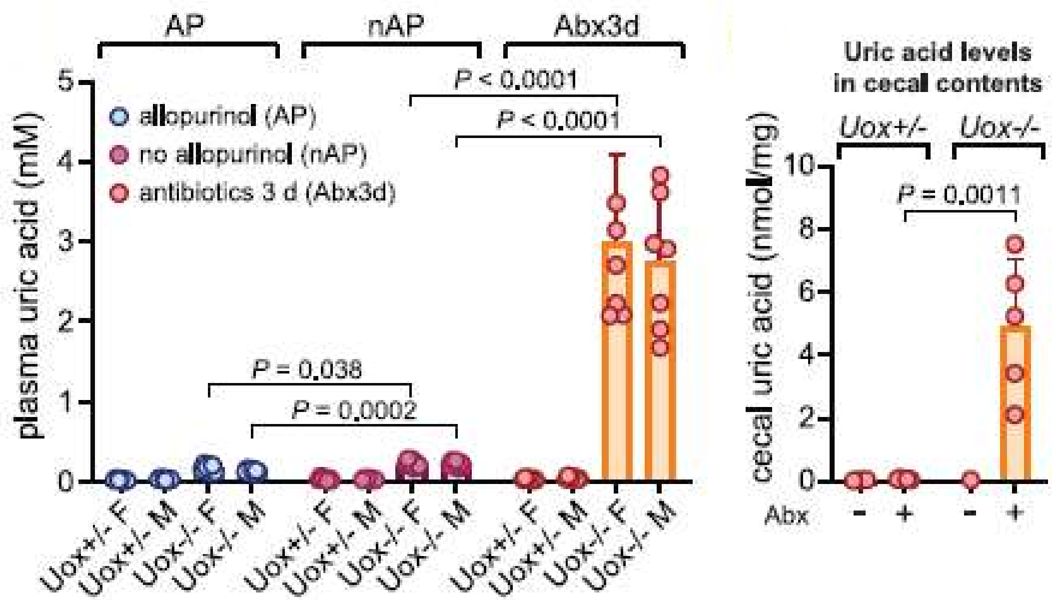
Cell

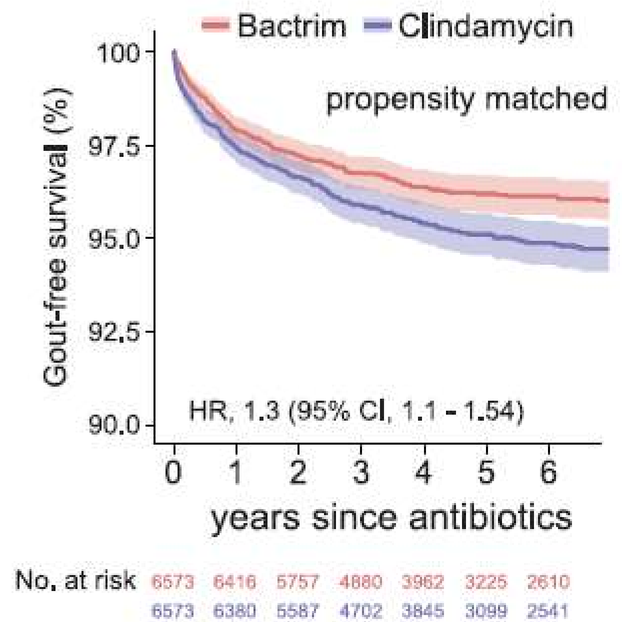
A widely distributed gene cluster compensates for uricase loss in hominids

Uox experimental design

Abx= antibiotic treatment







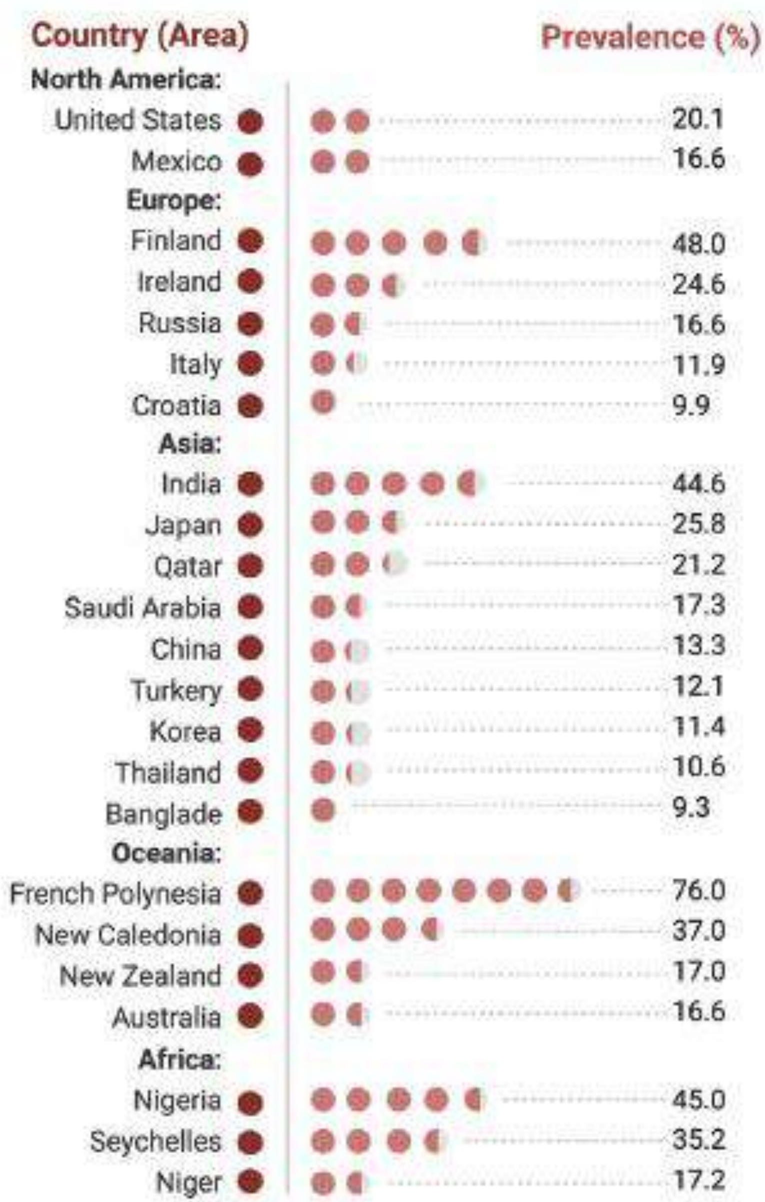
Chez l'Homme, clindamycine (bactéries anaérobies) ↑ 30% risque de goutte vs Bactrim

ATB uricase-/- → ↑ urate dans sang et sels

→ Déplétion de bactéries capables dégrader l'acide urique

Liu 2023

Hyperuricémie



Hyperuricémie ≥ 420 µmol/L

Prévalence monde : 9,3 - 76%

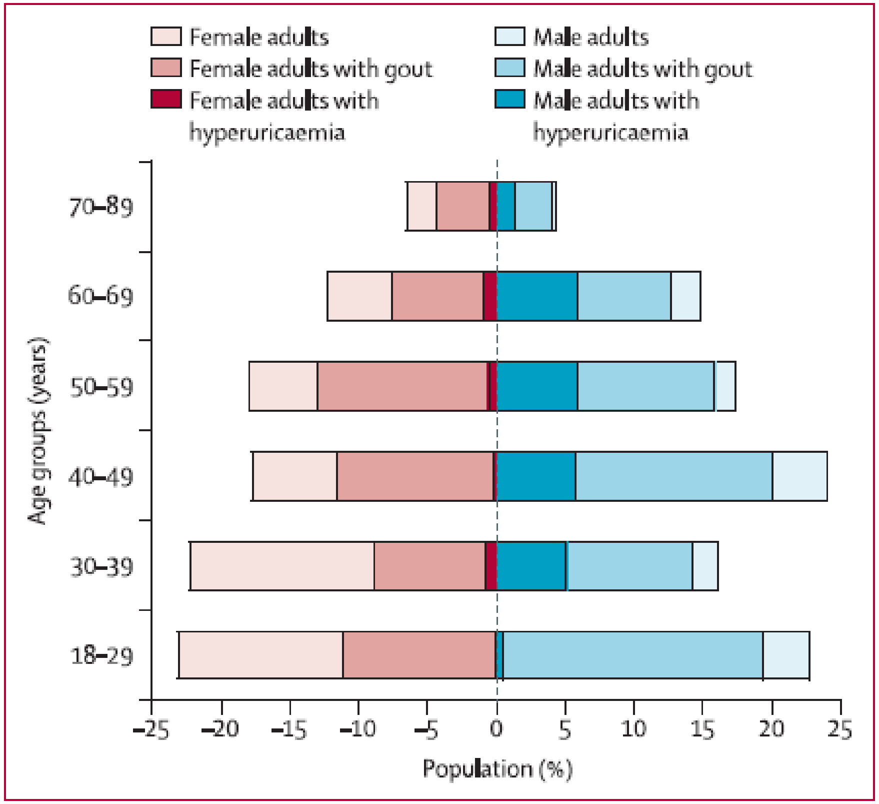
Prévalence Europe : 11,9- 48 %

Du 2024 Sign Transd Target Ther

The gout epidemic in French Polynesia: a modelling study of data from the Ma'i u'u epidemiological survey

Tristan Pascart, Kaja A Wasik, Cristian Preda, Valérie Chune, Jérémie Torterat, Nicolas Prud'homme, Maryline Nassih, Agathe Martin, Julien Le Masson, Vahinetua Rodière, Sylvain Frogier, Georges Canova, Jean-Paul Pescheux, Charles Shan Sei Fan, Charlotte Jauffret, Patrick Claeys, Sarah LeBaron von Baeyer, Stephane E Castel, Anne-Katrin Emde, Laura Yerges-Armstrong, Keolu Fox, Megan Leask, Jean-Jacques Vitagliano, Sahara Graf, Laurène Norberciak, Jacques Raynal, Nicola Dalbeth, Tony Merriman, Thomas Bardin, Erwan Oehler

Lancet Global Health 2024



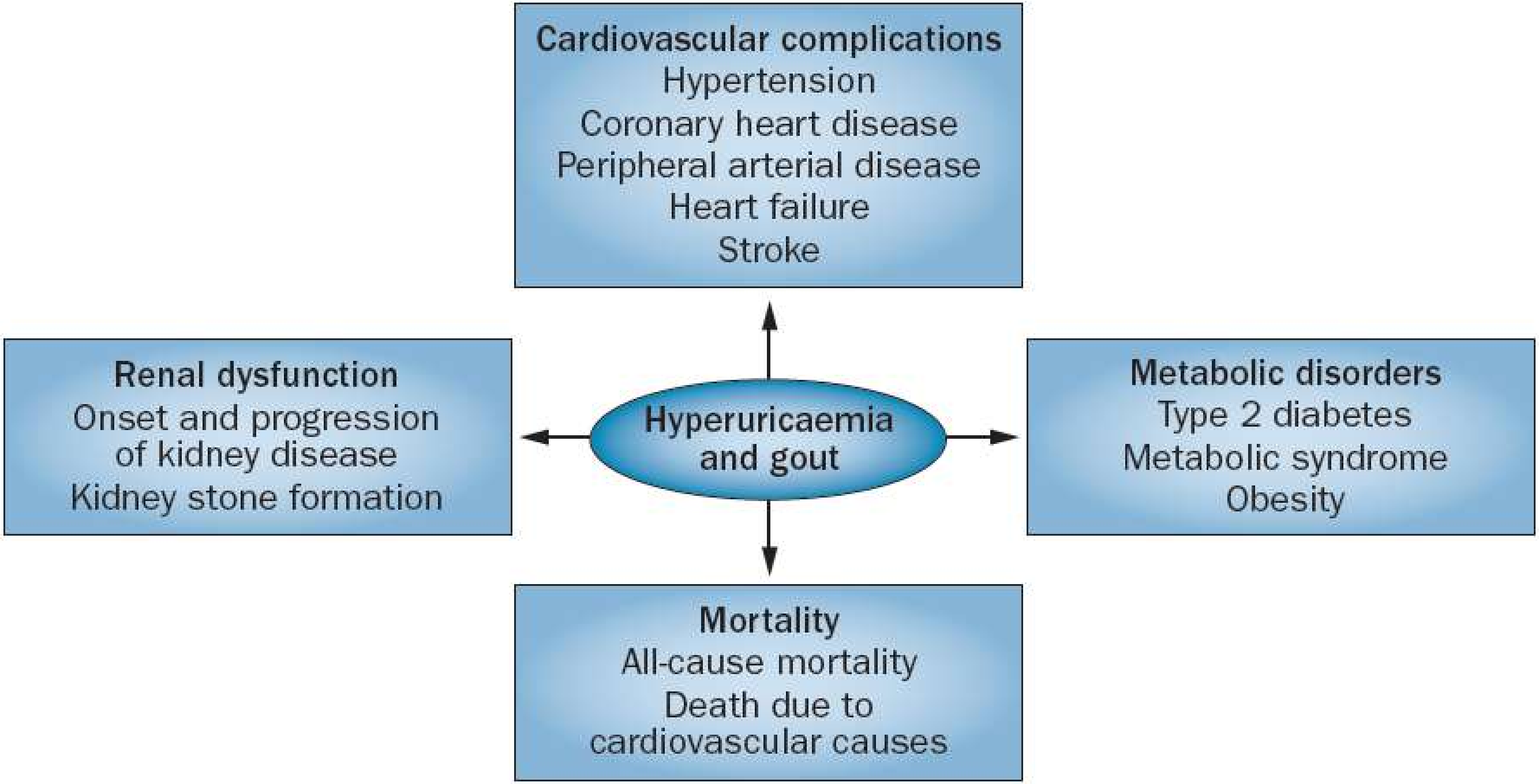
Goutte : 15,7% (3,5% F; 25,5% H)

Hyperuricémie : 71,6%

Chez pts goutte :

Obésité (70%),
HTA (77,2%),
DT2 (22,7%),
MRC 3-5 (9,7%)
CV (4,3%)

Hyperuricémie, goutte et Sd métabolique



Richette 2014 Nat Rev Rheum

Hyperuricémie : principal facteur de risque de la goutte

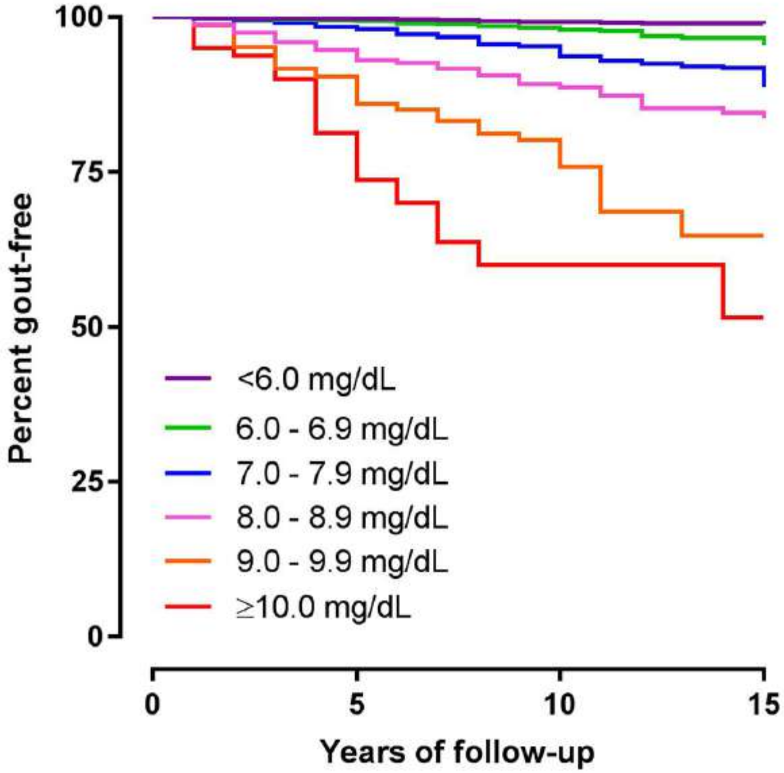
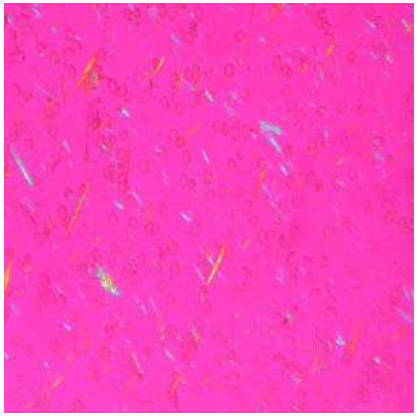


Figure 1 Kaplan-Meier plot showing the percentage of participants who were gout-free over the follow-up period, based on baseline serum urate categories in mg/dL.

Dalbeth 2018 Ann Rheum Dis



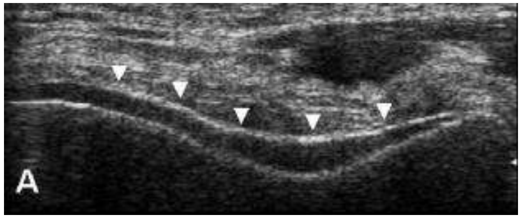
HK Ea

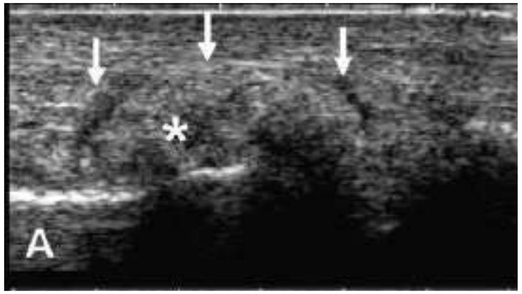
Schauer 2014 Nat Med

Cependant, seulement 15-30% des patients avec hyperuricémie développent une goutte

Crystal arthropathies

Musculoskeletal ultrasound findings in people with asymptomatic hyperuricemia: baseline analysis from the Transitions in Gout Research (TIGER) study using the OMERACT gout ultrasound semiquantitative scoring system





269 participants, uricémie > 480 µmol/L

Echographie : tendons patellaires, MTP1, tendons d'Achille

Résultats

DC certain (score >1) : 28.6%

Tophus : 17.1%

38.7 % avaient soit DC soit Tophus

Agrégats 38.1

Erosion osseuse 11.9%, hypertrophie synoviale 52.8% et inflammation synovial 5.2%

Que faire ? Faut-il initier THU chez patients avec dépôts asymptomatique ?

Stewart 2025 Ann Rheum Dis

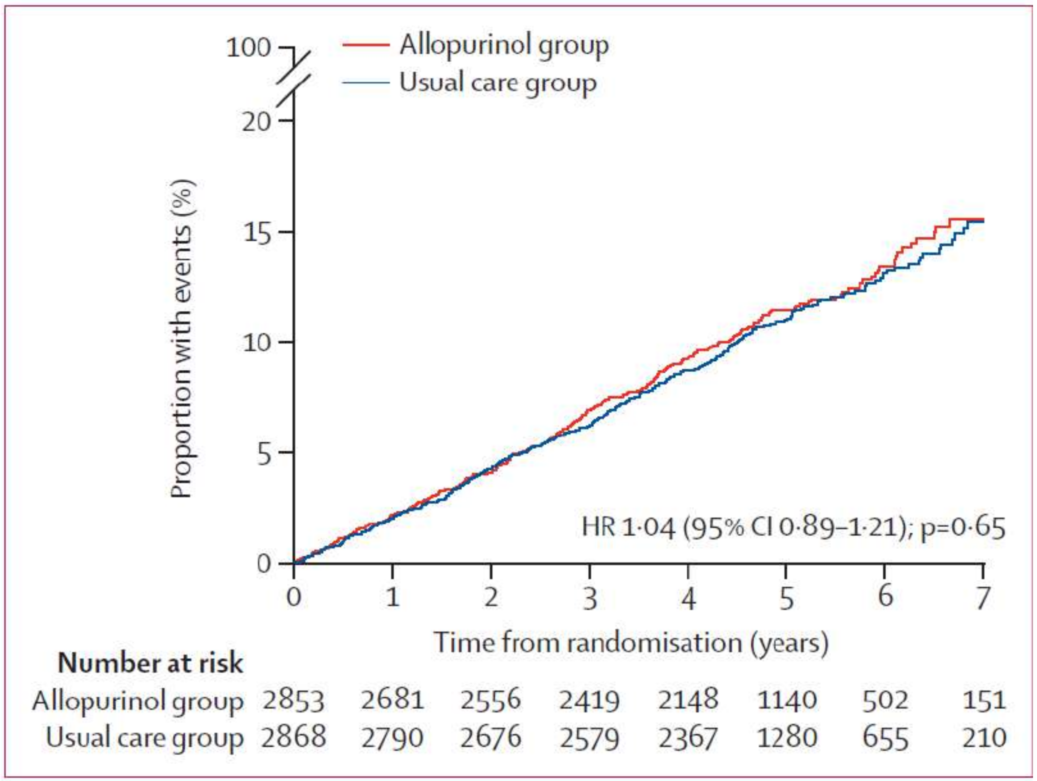
Merci de votre attention

Hôpitaux Universitaires
SAINT-LOUIS
LARIBOISIÈRE
FERNAND-WIDAL

Allopurinol versus usual care in UK patients with ischaemic heart disease (ALL-HEART): a multicentre, prospective, randomised, open-label, blinded-endpoint trial

Isla S Mackenzie, Christopher J Hawkey, Ian Ford, Nicola Greenlaw, Filippo Pigazzani, Amy Rogers, Allan D Struthers, Alan G Begg, L
Anthony J Avery, Jaspal S Taggar, Andrew Walker, Suzanne L Duce, Rebecca J Barr, Jennifer S Dumbleton, Evelien D Rooke, Jonathan
Lewis D Ritchie, Thomas M MacDonald, on behalf of the ALL-HEART Study Group*

2022



5721 participants, coronay disease,
Exclusion : gout, heart failure

Allopurinol (600 mg) *vs* usual care

Principal outcome: composite of non-fatal infarction, stroke and CV deaths

Non cardio-protective effect of allopurinol

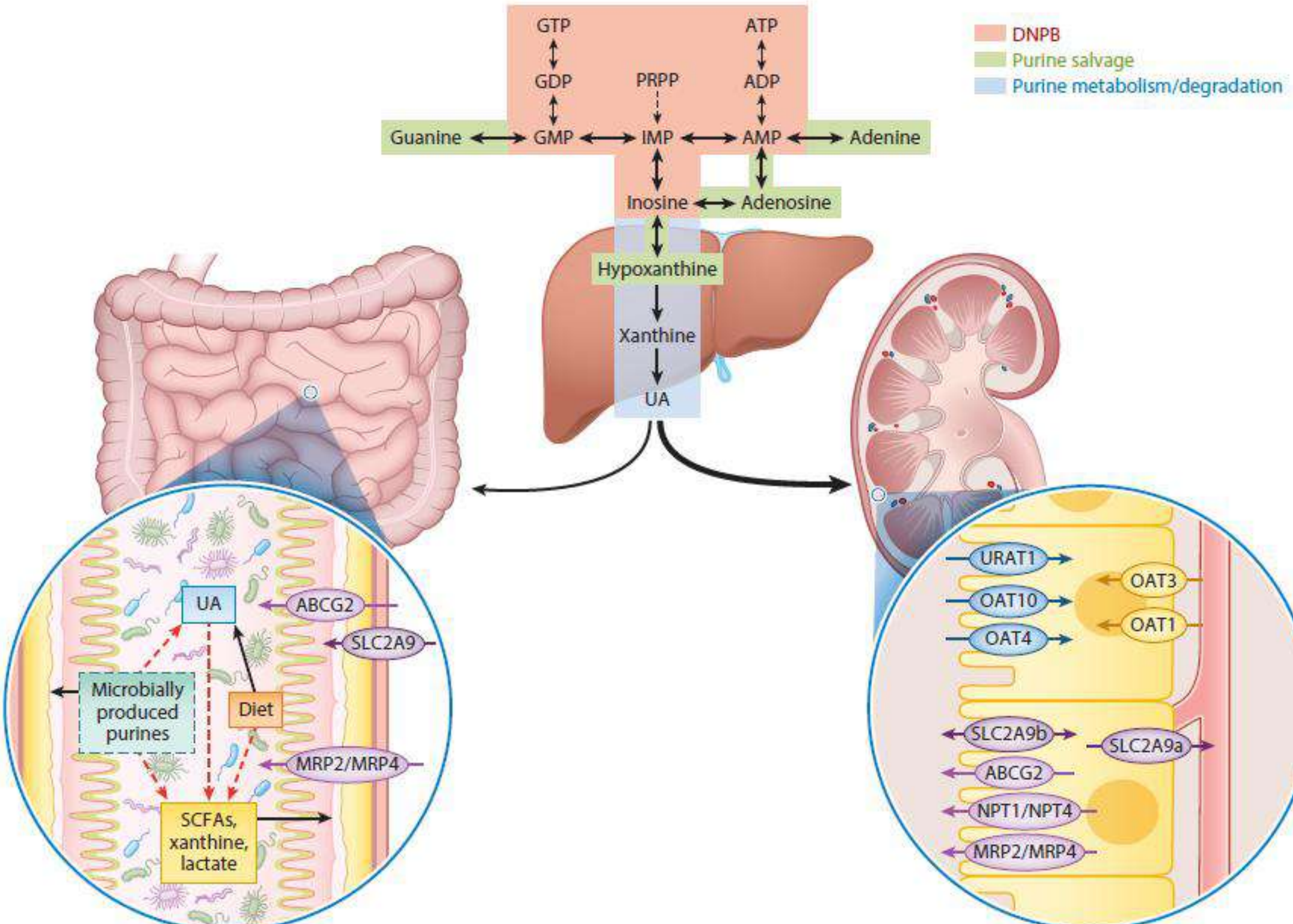
Limits:

Open study

57.4% withdrew allopurinol

Only 1/3 hyperucemia

No serum urate data



Emery 2025 Ann Rev Microbio

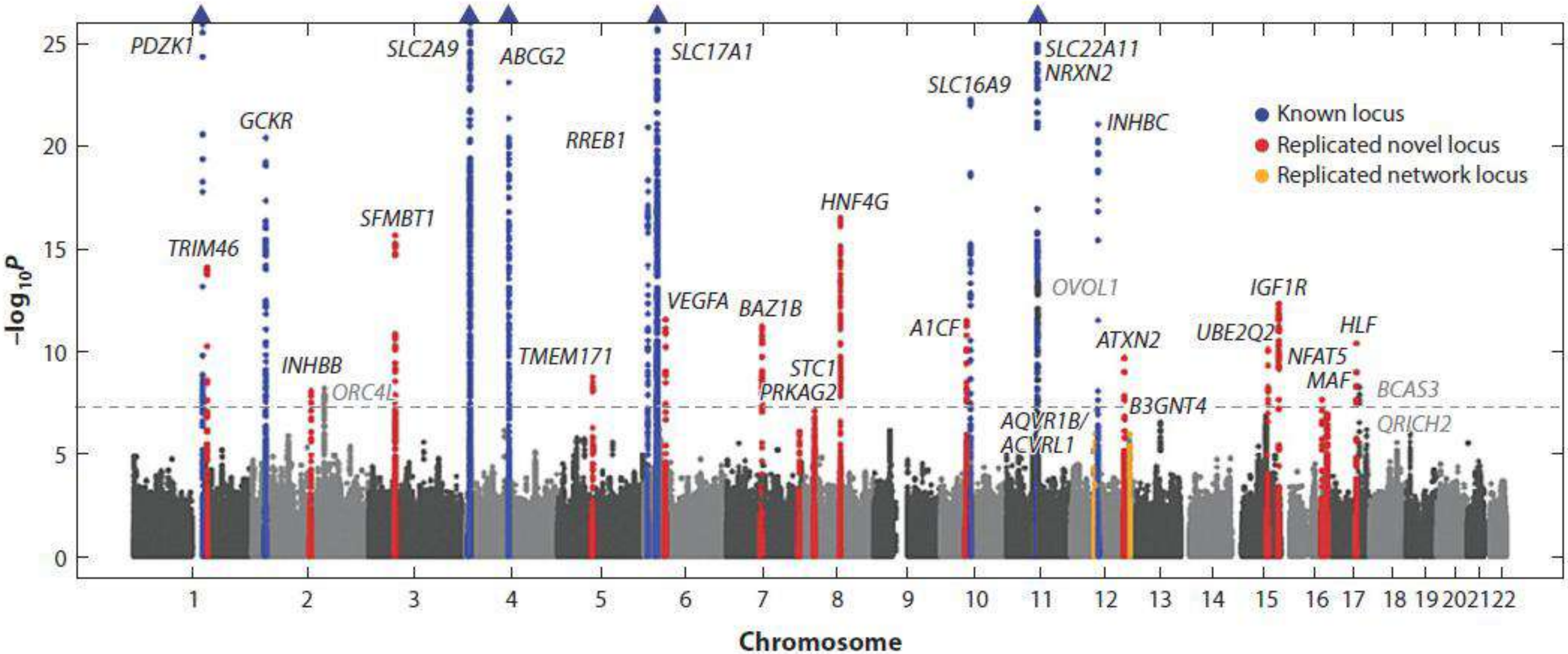


Figure 2

At least 28 genes affect the risk of hyperuricemia. A truncated Manhattan plot shows $-\log_{10}P$ values for all single-nucleotide polymorphisms (SNPs) of the urate discovery GWAS ordered by chromosomal position. The gene closest to the SNP with the lowest P value at each locus (index SNP) is listed. The loci in gray met one but not both replication criteria. Blue triangles represent loci containing SNPs with P values of less than 10^{-25}. From Reference 16.