St Mary's University Twickenham London

Genetic and physiological markers of salt sensitivity and its effects on salt taste perception and intake

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SCHOOL OF SPORT, HEALTH AND APPLIED SCIENCE

NuGO week 2017, Varna
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Outline

Background

- Hypertension and salt sensitivity (SS)
- Why salt taste perception and intake?

Part 1. SS, salt taste perception, salt intake

- Genetic predisposition to SS
- Genetic predisposition to impaired salt taste perception and increased salt intake

Part 2. Protein expression in SS

- SNP – protein expression
- Urinary exosome protein isolation and ELISA

Future prospects

- Future research on salt taste perception and intake
- SS biomarker?

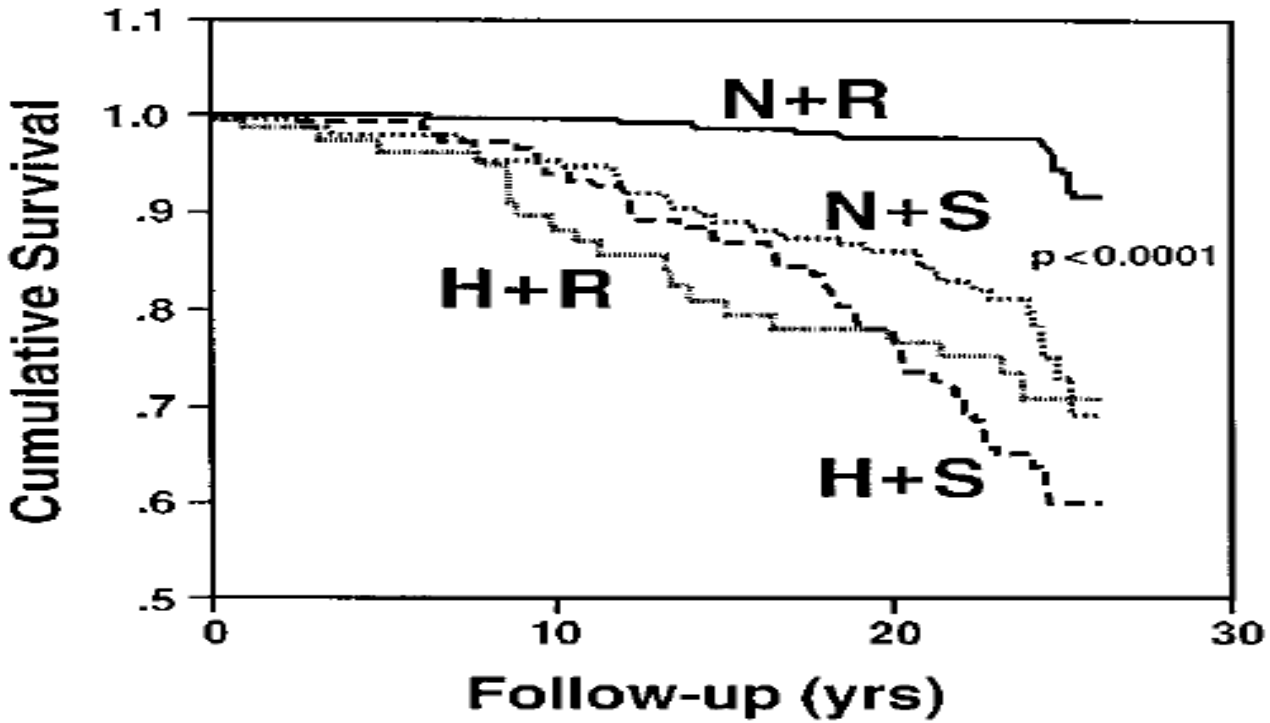
Hypertension

- Hypertension prevalence in Europe and globally 30-40%
- Hypertension responsible for at least 45% of deaths due to heart disease and 51% of deaths due to stroke
- Major contributor: excessive salt intake
- Salt intake in the EU ranging between 7 g and 18 g/day – exceeding recommended intake

WHO Regional office for Europe, 2013

Salt sensitivity

- Salt - induced increase in blood pressure
- 51% of hypertensive and 26% of people with normal blood pressure are salt-sensitive
- Independent CVD and mortality risk factor!



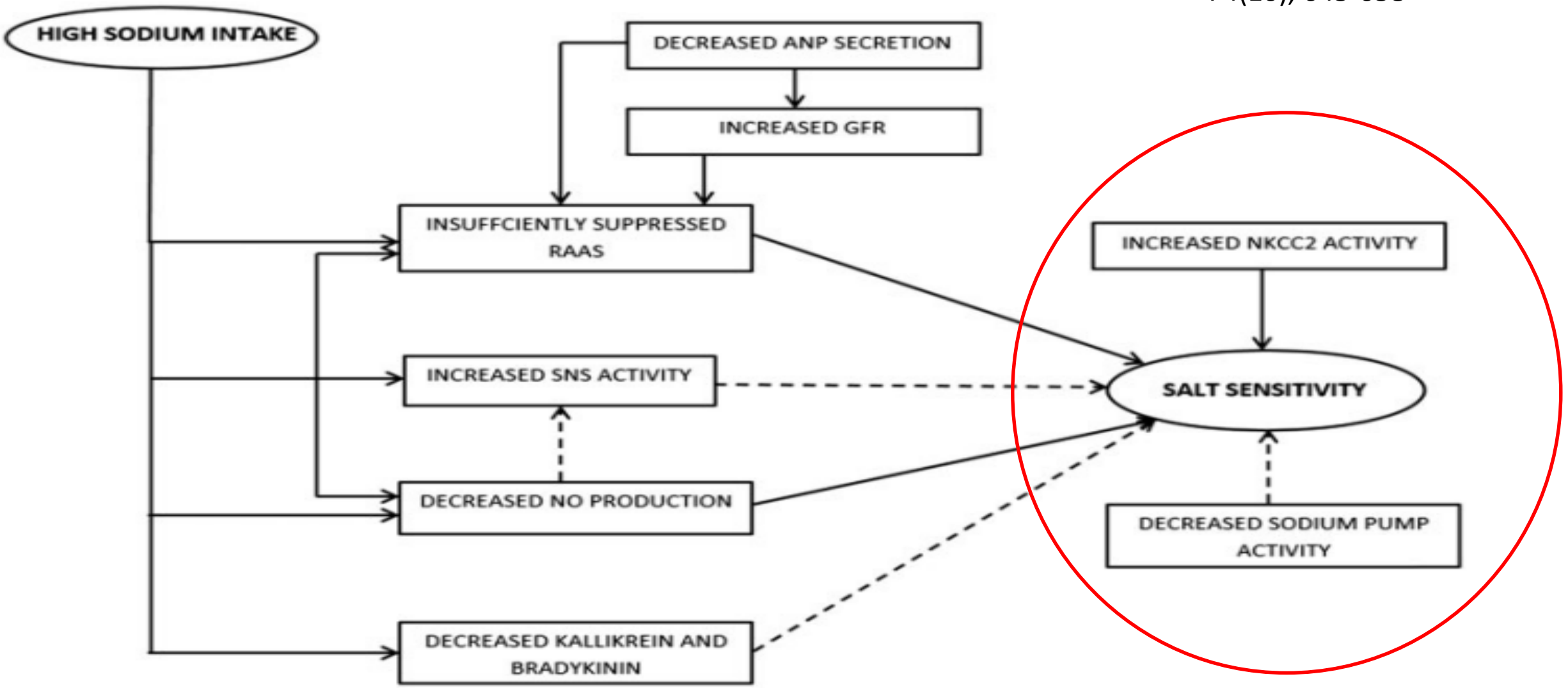
N – normal blood pressure
H – high blood pressure

R – salt-resistant
S – salt-sensitive

Weinberger et al. (2001) *Hypertension* 37, 429-432.

Interplay of mechanisms

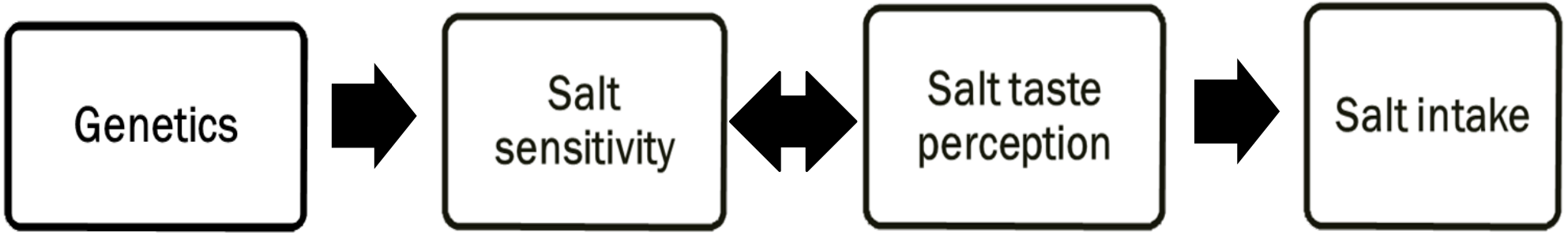
Pilic et al. (2016) *Nutr Rev* 74(10), 645-658



ANP, atrial natriuretic peptide; GFR, glomerular filtration rate; NKCC2, sodium-potassium-chloride cotransporter; NO, nitric oxide: RAAS, renin-angiotensin aldosterone system; SNS, sympathetic nervous system

Why salt taste perception/sensitivity and intake?

- Salt sensitivity – clear example of a gene-diet interaction
- Taste one of the main determinants of food intake
- Salt sensitivity suggested as the mediating variable in salt taste sensitivity – BP relationship
- Salt sensitivity, salt taste sensitivity (perception) and salt intake not studied comprehensively



Part 1.
Genetics of salt sensitivity and salt taste perception – the choice of SNPs

Gene	SNP	Outcome	Reference
SLC4A5 (electrogenic sodium bicarbonate cotransporter)	rs7571842 rs10177833	Blood pressure, pulse pressure, salt sensitivity (humans); may act jointly with ENaC (animals)	Carey et al., 2012 Hunt et al., 2006
SCNN1B (β-subunit of the ENaC)	rs239345	Salt taste suprathreshold sensitivity (humans), hypertension (humans)	Dias et al., 2013 Hannila-Handelberg et al, 2005
TRPV1 (ion channel/capsaicin receptor)	rs8065080	Salt taste suprathreshold sensitivity (humans), TRPV1 downregulation - salt sensitivity (animals)	Dias et al., 2013 Hao et al., 2011 Wang et al., 2006

Salt sensitivity status – AHA recommendations

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Genetic predisposition to salt sensitivity and its effects on dietary salt intake and hypertension

- Twenty healthy young to middle-aged subjects
- Low-salt diet for 7 days (3 g of salt/day)
- High-salt diet for additional 7 days (18 g salt/day)

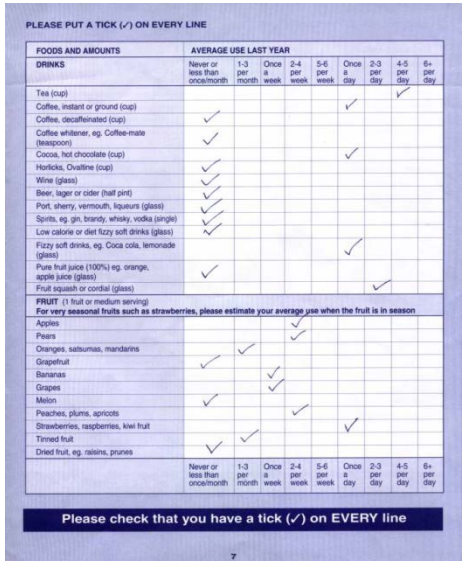
LOW SODIUM DIET PARTICIPANT BOOKLET

- **24-hour** automated blood pressure monitoring
- **24-hour** urine sample for sodium, potassium and creatinine excretion

Salt taste perception and intake

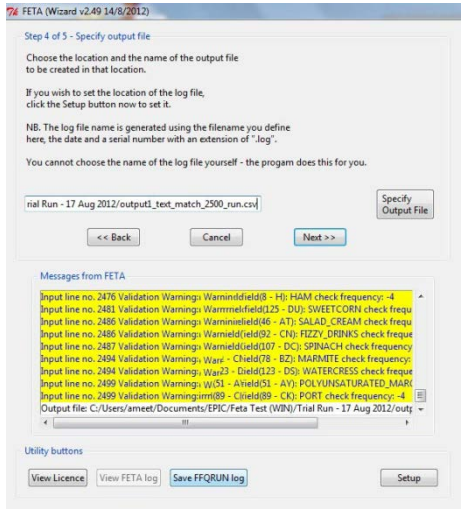
BS ISO3972:2011

STDT - the lowest concentration of the sample where the subject can consistently perceive an impression but not identify the taste.
STRT - the sample concentration where the subject consistently perceives the taste as salty.


PLEASE PUT A TICK (✓) ON EVERY LINE

FOODS AND AMOUNTS DRINKS	AVERAGE USE LAST YEAR: Never or less than once/month	1-3 per month	Once a week	2-4 per week	5-6 per week	Once a day	2-3 per day	4-5 per day	6+ per day
Tea (cup)								✓	
Coffee, instant or ground (cup)	✓					✓			
Coffee, decaffeinated (cup)	✓								
Coffee whitener, eg. Coffee-mate (teaspoon)	✓								
Cocoa, hot chocolate (cup)						✓			
Horlicks, Ovaltine (cup)	✓								
Wine (glass)	✓								
Beer, lager or cider (half pint)	✓								
Port, sherry, vermouth, liqueurs (glass)	✓								
Spirits, eg. gin, brandy, whisky, vodka (single)	✓								
Low calorie or diet fizzy soft drinks (glass)	✓								
Fizzy soft drinks, eg. Coca cola, lemonade (glass)						✓			
Pure fruit juice (100%) eg. orange, apple juice (glass)	✓								
Fruit squash or cordial (glass)							✓		
FRUIT (1 fruit or medium serving) **For very seasonal fruits such as strawberries, please estimate your average use when the fruit is in season**									
Apples				✓					
Pears				✓					
Oranges, satsumas, mandarins		✓							
Grapefruit	✓								
Bananas			✓						
Grapes			✓						
Melon	✓								
Peaches, plums, apricots				✓					
Strawberries, raspberries, kiwi fruit						✓			
Tinned fruit		✓							
Dried fruit, eg. raisins, prunes	✓								
	Never or less than once/month	1-3 per month	Once a week	2-4 per week	5-6 per week	Once a day	2-3 per day	4-5 per day	6+ per day

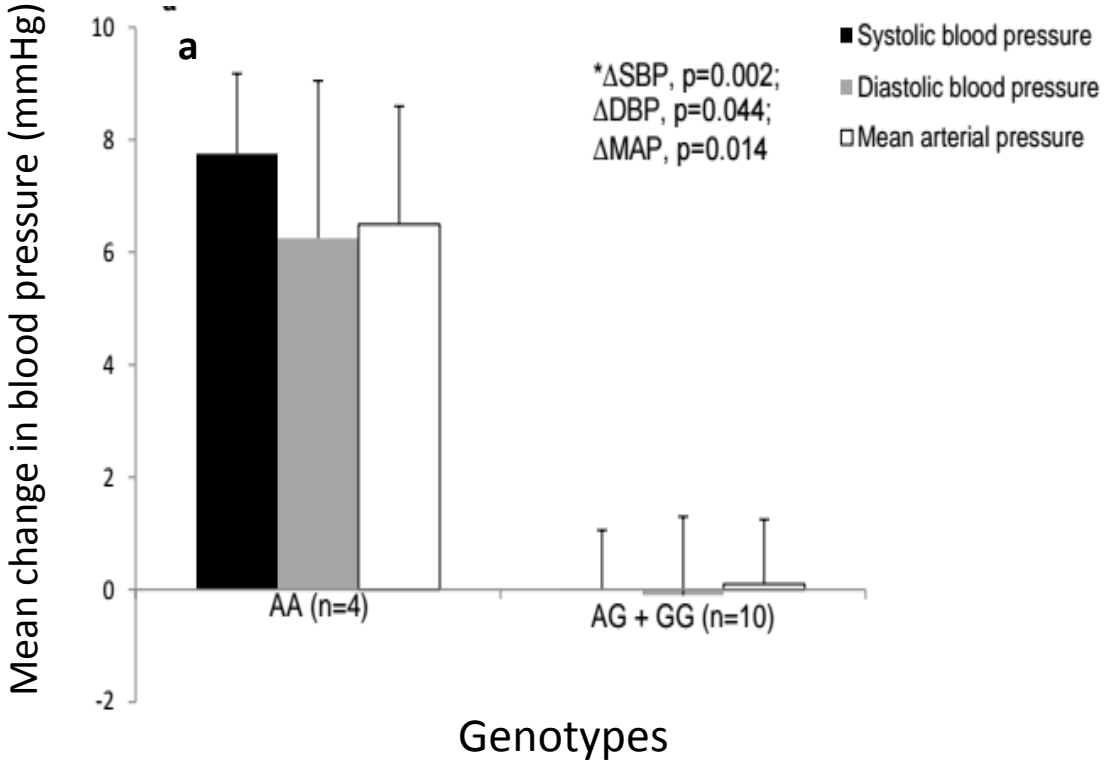
Please check that you have a tick (✓) on EVERY line



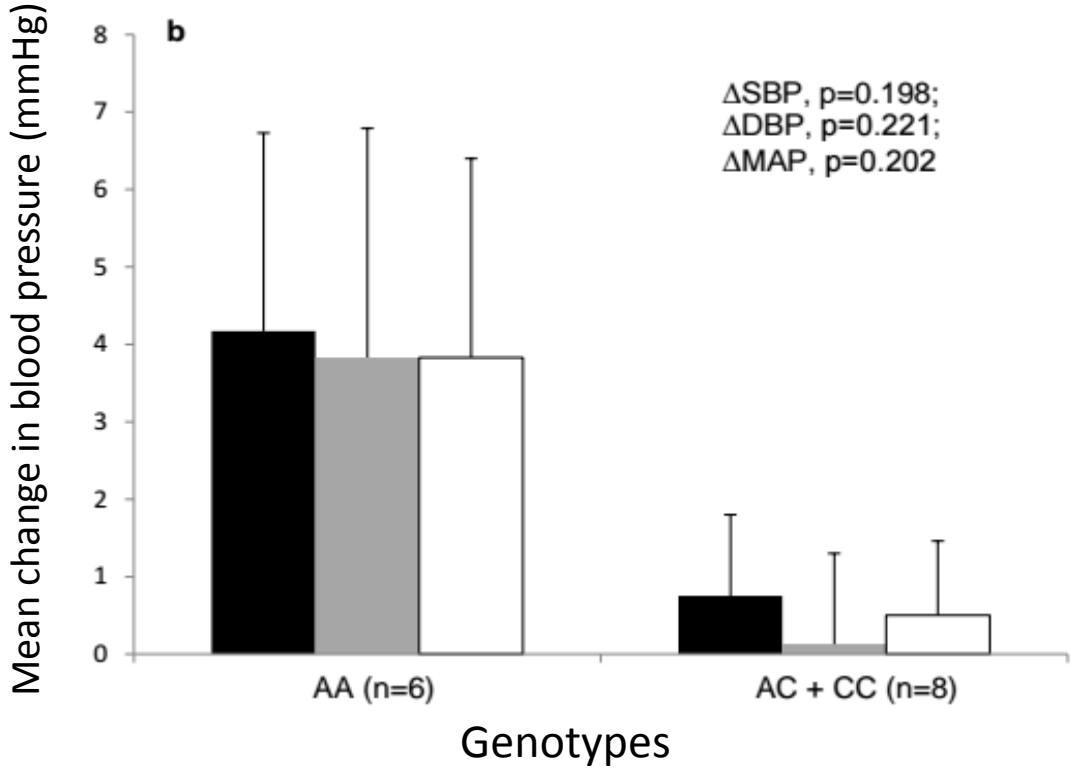
Salt intake (mg of sodium per 1000 kcal)

Genetic predisposition to salt sensitivity

rs7571842

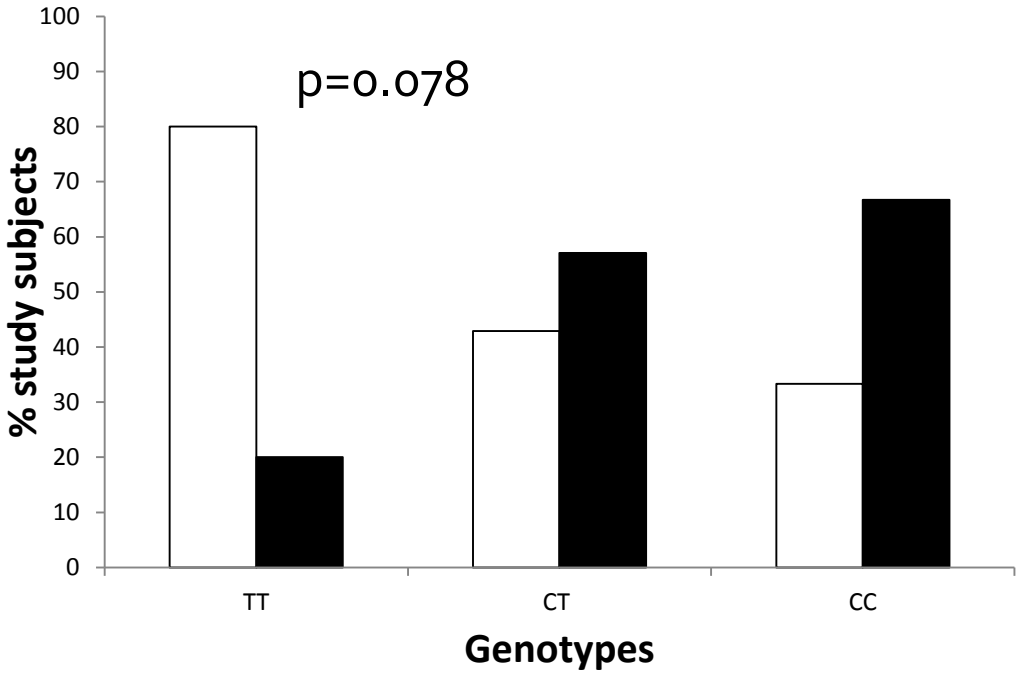


rs10177833



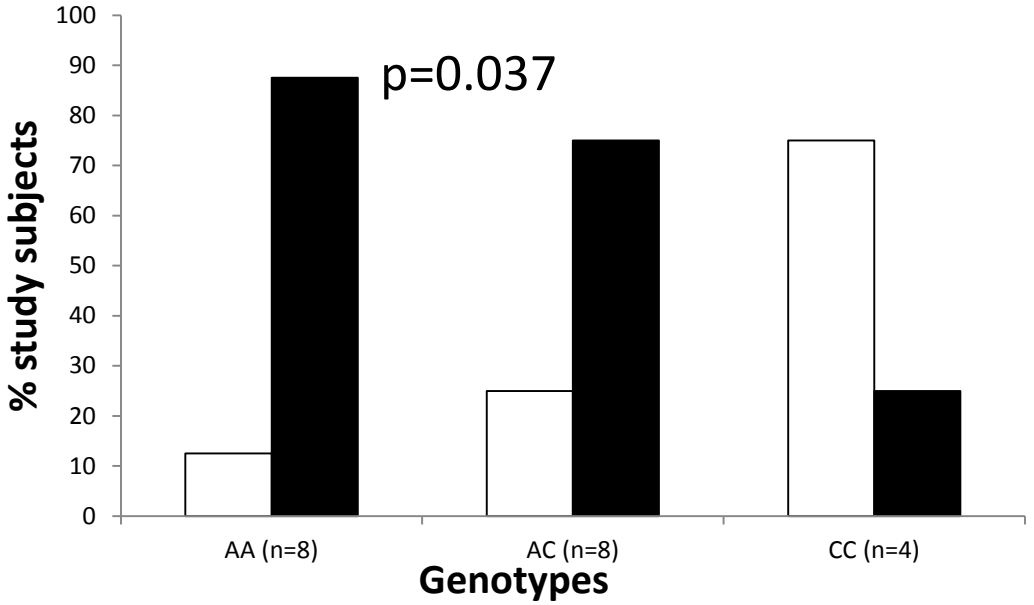
Genetics, salt taste perception and intake

TRPV1 rs8065080 – salt taste perception



Proportion of subjects (n=20) with low and high salt taste recognition thresholds

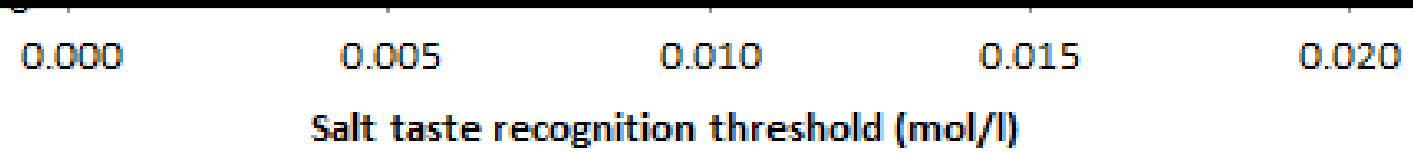
SLC4A5 rs10177833 – salt intake



Proportion of subjects (n=20) in different tertiles of sodium intake.

Associations between salt sensitivity, salt taste perception and salt intake

- SLC4A5 - salt-sensitive increase in BP, increased salt intake
- No association between genetics and salt taste perception
- Association between salt taste perception and intake depends on the genotype.
- Negative correlation between salt taste recognition threshold and the frequency of adding salt at the table in the rs8065080 TT group- preference for salty taste?



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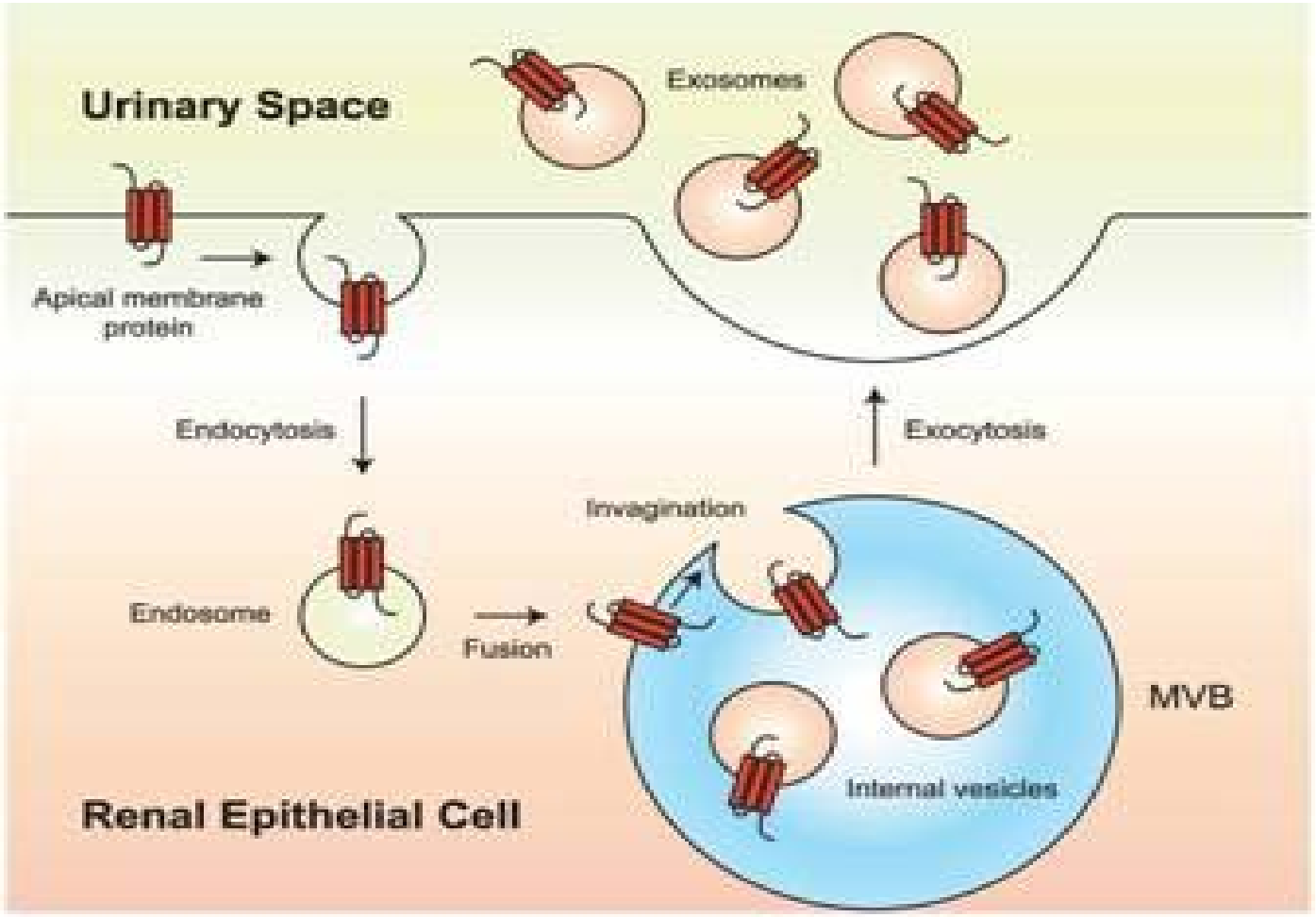
Part 2. Protein expression in salt sensitivity

- Sodium bicarbonate cotransporter (SLC4A5/NBCe2) as the protein of interest
- rs7571842 in strong LD with rs7583544 – transcriptional regulation? (F-SNP)

- Issues with salt sensitivity diagnosis
- Inability to conduct GWAS
- Genotype information not sufficient

Urinary exosome protein expression

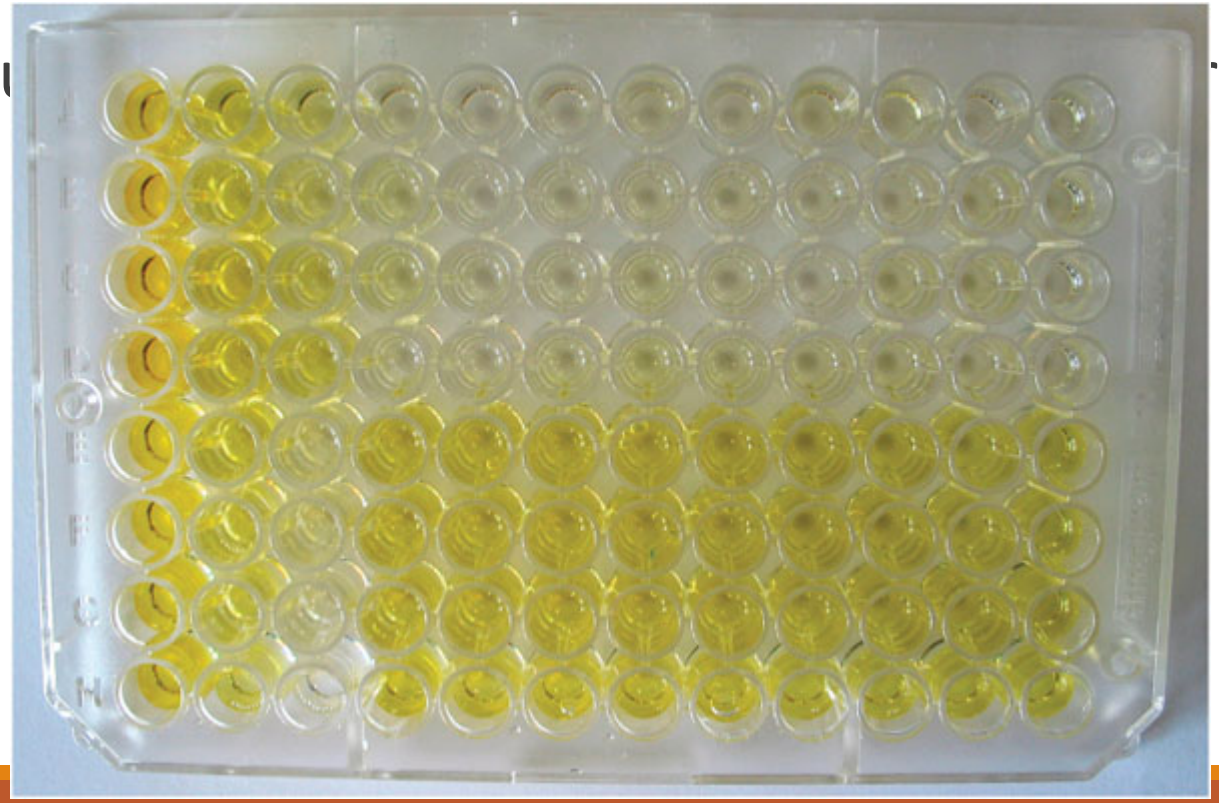


NIH Urinary exosome protein database

- NHE3, SLC4A4 and other members of the SLC family in the urinary exosome protein database
- SLC4A5?
- The aim: To isolate and measure the SLC4A5 protein expression from urinary exosomes and determine if there is a difference in expression according to rs7571842 genotype and salt sensitivity status

To date…

- Urine samples collected from 4 subjects diagnosed for salt sensitivity (rs7571842 AA and GG)
- Exosomes isolated u ruvanky et al. (2007)
- The ELISA issues
- But…



Nanomembrane concentrator

Future research

- Explore gene-gene interactions in salt sensitivity, salt taste sensitivity and salt intake (also causality and mechanism)
- A follow-up study utilising a different method of measuring salt intake
- Optimise the exosome isolation method for ELISA measurement – potential for salt sensitivity biomarker?

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