**Assignment brief**

SIW : MOLECULAR BASES OF PATHOLOGY

Integrated case of Genetics and Pharmacology

For SIW you have to work in groups that you usually study with (10-12 students in each group). You need to find articles on pharmacogenetics (at least one article per student) to research a particular topic, and summarise all of the information from those papers into one thesis. Potential topics that you can choose listed in the table (Attachment 2). Everyone’s contribution is crucial because everyone has to fill in the table in the attachment. It is one table per group, where each student brings in at least 1 paper that he/she researched and includes the main points from there such as:

* Topic
* Author, journal
* Hypotheses
* Methodology and materials
* Results
* Conclusion

Use Google scholar (<https://scholar.google.com/>) to search for reliable scientific papers. SIW will be in the form of a scientific conference in week 7, but the thesis and the table are due for submission by the **10th of October no later than 12.00**. Your thesis **must not exceed** **1000 words** including a reference list (approximately 2 pages).

An anti-plagiarism tool will be used. The acceptable percentage of plagiarism report in a research paper is **not more than 25% of similarity.**

The five best theses will be accepted for further presentation sessions, which will be held on Wednesday, 12th of October. There will be the following mark categories:

* **90 – 100%** for five selected groups who presented their thesis
* **50 – 80%** for other works
* **0%** Works that could not pass the anti-plagiarism test

This assignment will account for **9 marks** of the course mark

Two consulting sessions with a tutor will be held in week 6 and week 7, where you can get feedback on your current progress.

Assessment criteria for thesis and table (See attachment 3 for more details):

* Respond to or initiate research and clarify or determine what knowledge is required, heeding ethical/cultural and social/team considerations.
* Find and generate needed information/data using appropriate methodology.
* Determine and critique the degree of credibility of selected sources and of data generated, and reflect on the research processes used.
* Organise information and data to reveal patterns and themes, and manage teams and research processes.
* Analyse information/data critically and synthesise new knowledge to produce coherent individual/team understandings
* Write, present and perform the processes, understandings and applications of the research, and respond to feedback, accounting for ethical, social and cultural (ESC) issues.
* Inclusion of references and links to scientific papers, original sources that the reader can explore to follow up and understand your thesis.

Reference

1. www.pharmgkb.org/vips
2. Goodman and Gilman Basics of Therapeutics 2010, 2018
3. Pubmed. Ncbi
4. https://www.pharmgkb.org/vips

Assessment criteria for presentation:

| **Level of Achievement** | **Excellent** | **Good** | **Marginal** | **Inadequate** |
| --- | --- | --- | --- | --- |
| Organization  | • Well thought out with logical progression• Use of proper language• Significance clearly stated• Content level appropriate for audience• Abstract and bibliography are well constructed  | • Talk easy to follow• Use of proper language• Significance clearly stated• Content level not always appropriate• Abstract and/or bibliography have some errors  | • Talk somewhat disorganized• Shows some effort to use proper language• Significance somewhat unclear• Includes some irrelevant content and inappropriate content level• Abstract and bibliography are not well constructed | • Talk difficult to follow• Unclear language• Does not understand significance of work• Inadequate content• Abstract and bibliography lack proper content and construction  |
| Understanding of Scientific Content  | • Identifies the research question/research field• Has advanced understanding of the experimental approach and significance• Critically evaluates results, methodology and conclusions• Scientifically rigorous and well researched | • Identifies the research question/research field• Has basic understanding of the experimental approach and significance• Limited evaluation of results, methodology and conclusions• Well researched  | • Research question/research field somewhat unclear• Description of experimental approach somewhat confusing• Results and conclusions stated but not critically evaluated• Does not integrate outside readings | • Does not understand the research• Does not understand the experimental approach• Does not understand conclusions or recognize implications for future work  |
| Style/Delivery  | • Uses time wisely• Speaks with good pacing and enthusiasm• Makes eye contact and does not read information• Uses engaging tone and appropriate vocabulary  | • Speaks well, but often repeats comments• Exhibits few disfluencies (“ahs”, “uhms”, etc.)• Makes eye contact• Uses good vocabulary and tone  | • Presentation poorly timed• Some hesitation and uncertainty are apparent• Exhibits many disfluencies• Makes little eye contact and looks at notes• Monotone and nonengaging delivery | • Presentation poorly timed •Makes no eye contact and reads from notes• Hesitation and uncertainty are very apparent• Speaks too quietly or quickly for audience to hear and understand |
| Use of Visual Aids  | • Tables/graphs summarize data and/or conclusions• Size and labels are clear • Very little text• Figures and images explained and described well• Presentation has no misspellings or grammatical errors• Makes limited and effective use of laser pointer• AV set up properly  | • Text appropriately sized• Very little text• Most figures and images explained and described well• Presentation has an occasional misspelling or grammatical error • Uses laser pointer effectively • AV set up properly  | • Labels and legends somewhat unclear• Text size somewhat small• Too much detail on slides• Blocks of text on slides• Figures are explained• Presentation has multiple misspellings and/or grammatical errors• Uses laser pointer unnecessarily• AV mishaps resolved  | • Labeling is not clear• Size is too small to see• No logical placement of information• Mostly text and very few images• Figures are not explained • Presentation has numerous misspellings and/or grammatical errors• Use of laser pointer is distracting• AV mishaps unresolved |
| Ability to Answer Questions  | • Anticipates audience questions• Understands audience questions• Can integrate knowledge to answer questions • Thoroughly responds to questions | • Does not anticipate audience questions• Understands audience questions• Can integrate knowledge to answer questions • Thoroughly responds to most questions | • Does not anticipate audience questions• Makes an effort to address question• Can address some questions• Often responds poorly to questions  | • Either makes no effort to respond to questions or does so poorly  |

*Attachment 1*

| N | Student’s name |  | Reference to a paper (authors, theme, journal) | Hypotheses of research | Methods | Results | Conclusion |
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| 1 | 1 sample | Polymorphism in the beta(1)-adrenergic receptor gene and hypertension | [K Bengtsson](https://pubmed.ncbi.nlm.nih.gov/?term=Bengtsson+K&cauthor_id=11447084) [1](https://pubmed.ncbi.nlm.nih.gov/11447084/#affiliation-1), [O Melander](https://pubmed.ncbi.nlm.nih.gov/?term=Melander+O&cauthor_id=11447084), [M Orho-Melander](https://pubmed.ncbi.nlm.nih.gov/?term=Orho-Melander+M&cauthor_id=11447084), [U Lindblad](https://pubmed.ncbi.nlm.nih.gov/?term=Lindblad+U&cauthor_id=11447084), [J Ranstam](https://pubmed.ncbi.nlm.nih.gov/?term=Ranstam+J&cauthor_id=11447084), [L Råstam](https://pubmed.ncbi.nlm.nih.gov/?term=R%C3%A5stam+L&cauthor_id=11447084), [L Groop](https://pubmed.ncbi.nlm.nih.gov/?term=Groop+L&cauthor_id=11447084) | polymorphism is associated with hypertension in Scandinavians | A total of 292 unrelated, nondiabetic, hypertensive patients and 265 unrelated healthy control subjects were included in a case-control association study.From 118 families, 102 nondiabetic sibling pairs without antihypertensive medication who were discordant for the Arg389Gly polymorphism were selected for a sibling study. Allele and genotype frequencies of the Arg389Gly and Ser49Gly polymorphisms were compared between hypertensive patients and normotensive control subjects.Blood pressure and heart rate were compared between carriers of the different genotypes.  | In the case-control study, the age- and body mass index-adjusted odds ratio for hypertension in subjects homozygous for the Arg389 allele was 1.9 (95% confidence interval, 1.3 to 2.7; P=0.0005) when compared with carriers of 1 or 2 copies of the Gly389 allele. The genotype-discordant sibling pair analysis revealed that siblings homozygous for the Arg389 allele had significantly higher diastolic blood pressures (79.4+/-9.9 versus 76.0+/-10.1 mm Hg; P=0.003) and higher heart rates (68.3+/-11.0 versus 65.1+/-9.4 bpm; P=0.02) than siblings carrying 1 or 2 copies of the Gly389 allele. The Ser49Gly polymorphism was not associated with hypertension. | Our data suggest that individuals homozygous for the Arg389 allele of the beta(1)-adrenergic receptor gene are at increased risk to develop hypertension. |
| 2 | 2  | β-Adrenergic Receptor Gene Polymorphisms and β-Blocker Treatment Outcomes in Hypertension | [MA Pacanowski](https://pubmed.ncbi.nlm.nih.gov/?term=Pacanowski%20M%5BAuthor%5D),1 [Y Gong](https://pubmed.ncbi.nlm.nih.gov/?term=Gong%20Y%5BAuthor%5D),1 [RM Cooper-DeHoff](https://pubmed.ncbi.nlm.nih.gov/?term=Cooper-DeHoff%20R%5BAuthor%5D),2 [NJ Schork](https://pubmed.ncbi.nlm.nih.gov/?term=Schork%20N%5BAuthor%5D),3 [MD Shriver](https://pubmed.ncbi.nlm.nih.gov/?term=Shriver%20M%5BAuthor%5D),4 [TY Langaee](https://pubmed.ncbi.nlm.nih.gov/?term=Langaee%20T%5BAuthor%5D),1 [CJ Pepine](https://pubmed.ncbi.nlm.nih.gov/?term=Pepine%20C%5BAuthor%5D),2 and [JA Johnson](https://pubmed.ncbi.nlm.nih.gov/?term=Johnson%20J%5BAuthor%5D)1,2,  | β1- and β2-adrenergic receptor gene (*ADRB1* and *ADRB2*) variants influence cardiovascular risk and β-blocker responses in hypertension and heart failure | We evaluated the relationship between *ADRB1* and *ADRB2* haplotypes, cardiovascular risk (death, nonfatal myocardial infarction (MI ), and nonfatal stroke), and atenolol-based vs. verapamil sustained-release (SR )-based antihypertensive therapy in 5,895 coronary artery disease (CAD) patients.  | After an average of 2.8 years, death rates were higher in patients carrying the *ADRB1* Ser49-Arg389 haplotype (hazard ratio (HR ) 3.66, 95% confidence interval (95% CI) 1.68–7.99). This mortality risk was significant in patients randomly assigned to verapamil SR (HR 8.58, 95% CI 2.06–35.8) but not atenolol (HR 2.31, 95% CI 0.82–6.55), suggesting a protective role for the β-blocker.  | *ADRB2* haplotype associations were divergent within the treatment groups but did not remain significant after adjustment for multiple comparisons. *ADRB1* haplotype variation is associated with mortality risk, and β-blockers may be preferred in subgroups of patients defined by *ADRB1* or *ADRB2* polymorphisms. |
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Attachment 2

Keywords on potential topics to choose

| Gene | Gene polymorphisms | Drugs  | Effect of polymorphisms on drugs efficiency  |
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| CYP2D6 |  | Amitriptyline, atomoxetine, bufuralol, bupranolol, carvedilol, chlorpheniramine, chlorpromazine, clomipramine, clozapine, codeine, debrisoquine, desipramine, dextromethorphan, dihydrocodeine, encainide, flecainide, fluoxetine, fluvox- amine, guanoxan, haloperidol, hydrocodone, imipramine, maprotiline, 4–methoxy-amphetamine, metoclopramide, metoprolol, mexiletine, nebivolol, nortriptyline, oxycodone, palonosetron, paroxetine, perhexiline, perphenazine, phen- formin, propafenone, propoxyphene, propranolol, risperi- done, selegiline (deprenyl), sparteine, tamoxifen, thioridazine, timolol, tolterodine, tricyclic antidepressants, tramadol, trazodone, venlafaxine  |  |
| CYP2C9 |  | Alosetron, bosentan, celecoxib, chlorpropamide, diclofenac, dronabinol, flurbiprofen, fluvastatin, glimepiride, glipizide, glyburide, hexobarbital, ibuprofen, indomethacin, irbesartan, losartan, meloxicam, montelukast, naproxen, nateglinide, phenobarbital, phenytoin, piroxicam, rosiglitazone, rosuvastatin, sulfamethoxazole, sulfaphenazole, ticrynafen, tolbutamide, torsemide, trimethadione, valsartan, *S*-warfarin |  |
| Glucose 6 phosphate dehydrogenase  |  | салицилаты |  |
| BCHE |  |  |  |
| [P2RY12 PGx](https://www.pharmgkb.org/vip/PA166169436) |  | ADP induced agregation |  |
| [KCNJ11 PGx](https://www.pharmgkb.org/vip/PA166169501)  |  | sulfonylureas |  |
| [CYP2E1](https://www.pharmgkb.org/vip/PA166169425) |  | Acetaminophen, chlorzoxazone, dacarbazine, enflurane, ethanol (a minor pathway), halothane, isoflurane, isoniazid, sevoflurane, theophylline, trimethadione |  |
| [CYP1A2 PGx](https://www.pharmgkb.org/vip/PA166165414) |  | caffeine and antipsychotics. |  |
| [ACE PGx](https://www.pharmgkb.org/vip/PA166165404) |  | ace inhibitors |  |
| [ADRB1 PG](https://www.pharmgkb.org/vip/PA166170369) |  | G-protein-coupled receptor expressed in cardiac tissue |  |
| [ADRB2 PGx](https://www.pharmgkb.org/vip/PA166165410) |  | beta-2-adrenergic receptor |  |
| [CACNA1S PG](https://www.pharmgkb.org/vip/PA166179230) |  | L-type calcium channel |  |

Attachment 3

