**LAB 3:** Construct and validate a genetic instrument ready for your own example

Programs to use: exposurex

There are several methods of creating genetic instruments. You could find genetic instruments from a previous publication, you could select on specific criteria, for example all the SNPs strongly associated with blood pressure from the *ACE* gene to provide a genetic mimic of ACE inhibitors, or you could create your own. MR-Base can do it for you very easily if your exposure GWAS is in MR-Base. So, to provide an example of doing it by hand, we will create instruments for a metabolite not in MR-Base, which we will use now, to obtain instruments for theobromine. Then we will have a look at the associations with IHD

MR estimate for theobromine on IHD

1. **SNPs to exposure**
   1. A publicly available GWAS, Long et al <https://www.ncbi.nlm.nih.gov/pubmed/28263315>, which can be found here <http://www.hli-opendata.com/Metabolome> has a GWAS of theobromine. We have extracted the GWAS elements relevant to theobromine, into a file called long-theobromine.txt
   2. Use this program “exposurex” to
      1. Install packages in R
      2. Read in the SNPs to exposure file
      3. Select SNPs with p-value<5x10-6
      4. Only keep uncorrelated SNPs
      5. Write out a CSV file for the SNPs (theobro.csv)
2. **Obtain estimates (method 1 using MR-base code and Mendelianrandomization) continue using the program “exposurex”**
   * 1. Use MR base to get information about IHD
     2. Use MR base to get MR estimates
     3. Use Mendelianrandomization to get MR estimates
3. **Obtain estimates (method 2 using MR base web interface)**
   * 1. Edit the file theobro.csv to have the right headings for MR Base
     2. Simply read the file theobro.csv into MR base and select the largest Nikpay Cardiogram file, and use MR-Base to obtain the estimate.
4. **Now answer the following questions**
   1. Do you think all the SNPs predicting theobromine are valid instruments? Please explain your answer.
   2. Based on your findings do you think theobromine causes IHD?
   3. Is there any other analysis you would like to do?