# The Association of Genetic Variants and Non-Genetic Factors with Efficacy of Clopidogrel in the Egyptian Population

**Thesis for partial fulfillment of PhD degree in pharmaceutical sciences (Biochemistry)**

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بسم الله الرحمن الرحيم

"سَنُرِيهِمْ آَيَاتِنَا فِي الآَفَاقِ وَفِي أَنْفُسِهِمْ
حَتَّى يَتَبَيَّنَ لَهُمْ أَنَّهُ الحَقُّ أَوَلَمْ يَكْفِ بِرَبِّكَ
أَنَّهُ عَلَى كُلِّ شَيْءٍ شَهِيد"

صدق الله العظيم

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***Basma F. Khalil***

# List of Abbreviations

| Abbreviation | Stands for |
|---|---|
| *ABCB1* | Adenosine Triphosphate (ATP)-Binding Cassette, Sub-Family B |
| AC | Adenylate Cyclase |
| ACC | American College of Cardiology |
| ACE | Angiotensin Converting Enzyme |
| ACS | Acute Coronary Syndrome |
| ACTIVE | Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events |
| ADP | Adenosine Diphosphate |
| AHA | American Heart Association |
| AMI | Acute Myocardial Infarction |
| APCs | Antigen-Presenting Cells |
| APS | Adenosine 5' Phosphosulfate |
| ARBs | Angiotensin Receptor Blockers |
| AST | Aspartate Aminotransferase |
| ATP | Adenosine Triphosphate |
| BAFF | B-cell Activating Factor |
| BMI | Body Mass Index |
| BNP | B-Natriuretic Peptide |
| bp | Base Pair |
| CABG | Coronary Artery Bypass Grafting |
| cAMP | Cyclic Adenosine Monophosphate |
| CD4 | Cluster of Differentiation 4 |
| CI | Confidence Interval |
| CK | Creatine Kinase |
| CK-MB | Creatine Kinase (Cardiac isoenzymes) |
| $CK\text{-}MB_{1 \text{ and } 2}$ | Creatine Kinase isoforms |
| COX-1 | Cyclo-Oxygenase 1 |

| Abbreviation | Stands for |
|---|---|
| CPIC | Clinical Pharmacogenetics Implementation Consortium |
| CRP | C-Reactive Protein |
| cTn | Cardiac Troponin |
| cTnI | Cardiac Troponin I |
| cTnT | Cardiac Troponin T |
| CVD | Cardiovascular Diseases |
| CURE | Clopidogrel in Unstable Angina to Prevent Recurrent Events |
| *CYP2C19* | Cytochrome P450 2C19 |
| *CYP450* | Cytochrome P450 |
| DC | Dendritic Cells |
| DNA | Deoxyribonucleic Acid |
| dNTP | Deoxyribonucleotide Triphosphate |
| ECG | Electro-Cardiogram |
| EM | Extensive Metabolizers |
| ER | Endoplasmic Reticulum |
| ESC | European Society of Cardiology |
| FAST-MI | French Registry of Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction |
| FDA | Food and Drug Administration |
| GDF-15 | Growth Differentiation Factor-15 |
| GP | Glycoprotein |
| GPBB | Glycogen Phosphorylase Isoenzyme in Brain and Heart |
| GWAS | Genome-Wide Association Studies |
| H-FABP | Heart Fatty Acid Binding Protein |
| hs-CRP | High Sensitive C-Reactive Protein |
| hs-Tn | High Sensitivity Tn |
| IL | Interleukin |
| IM | Intermediate Metabolizers |

| Abbreviation | Stands for |
|---|---|
| IFN-γ | Interferon-Gamma |
| IHD | Ischemic heart disease |
| LDH | Lactate Dehydrogenase |
| LOF | Loss-of-Function Allele |
| MACE | Major Adverse Cardiac Events |
| MAF | Minor Allele Frequencies |
| MDRS | MPO-Derived Reactive Species |
| MI | Myocardial Infarction |
| MMPs | Matrix Degrading Metalloproteinases |
| MPO | Myeloperoxidase |
| MDR1 | Multi-Drug Resistance 1 Protein |
| NETs | Neutrophil Extracellular Traps |
| NGS | Next Generation DNA Sequencing |
| NLRP | Nucleotide-binding domain and Leucine-Rich repeat containing Proteins |
| NSTEMI | Non-ST Elevation Myocardial Infarction |
| OPR | On-treatment Platelet Reactivity |
| OR | Odd Ratio |
| PAI-1 | Plasminogen Activator Inhibitor-1 |
| PAR | Platelet Protease-Activated Receptor |
| PCI | Percutaneous Coronary Interventions |
| PCR | Polymerase Chain Reaction |
| PD | Pharmacodynamics |
| PDE-3 | Platelet Phosphodiesterase-3 |
| P-GP | Permeability G-protein |
| PK | Pharmacokinetics |
| P2Y12 | ADP platelets receptor |
| PLATO | Platelet Inhibition and Patient Outcomes |
| PM | Poor Metabolizers |
| PMN | Polymorphonuclear Leukocytes |

| Abbreviation | Stands for |
|---|---|
| PPIs | Proton Pump Inhibitors |
| PPi | Pyrophosphate |
| RBG | Random Blood Glucose |
| SNPs | Single Nucleotide Polymorphisms |
| STEMI | ST Elevation Myocardial Infarction |
| TAE | Tris/Acetate/EDTA buffer |
| Th | T helper Lymphocytes |
| TGF-β | Transforming Growth Factor-βeta |
| TLR | Toll-Like Receptor |
| Tn | Troponin |
| Tn (I, C, T) | Troponin isoforms |
| TNF | Tumor Necrosis Factor |
| TPβ | Thromboxane Receptor |
| tPA | Tissue-type Plasminogen Activators |
| Treg | Regulatory T cells |
| TRITON-TIMI 38 | Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis In Myocardial Infarction |
| TXA2 | Thromboxane A2 |
| UA | Unstable Angina |
| UM | ultrarapid metabolizers |
| uPA | Urokinase-type Plasminogen Activators |
| VASP | Vasodilator-Stimulated Phosphoprotein |
| VASP-P | Phosporylated Vasodilator-Stimulated Phosphoprotein |
| vWF | von Willebrand Factor |
| WHO | World Health Organization |

# Table of Contents

# List of Figures