PI profile

## Nicky Whiffin

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|  | **Dr. Nicky Whiffin**  **Titles**: Group Leader / Sir Henry Dale Fellow  **Location**: Wellcome Centre for Human Genetics  **Department**: Nuffield Department of Medicine  **Group**: Computational Rare Disease Genomics  **Webpage**: [www.rarediseasegenomics.org](http://www.rarediseasegenomics.org)  **Email**: [nwhiffin@well.ox.ac.uk](mailto:nwhiffin@well.ox.ac.uk) |

### GMS themes:

* Genome biology (genomes and genetic variation)
* Genomics of disease
* Genomic analysis (bioinformatics and statistical genetics)
* Application of genomics in the clinic (diagnostics and therapeutics)

### Research Overview

Although individually rare (affecting <1/2000 individuals) collectively, rare diseases affect >250 million people globally. Identifying the genetic cause of disease is of huge benefit to both patients and their families; allowing screening of additional family members to identify those also at risk, enabling return of an accurate diagnosis to the patient, and dictating personalised treatment approaches. Clinical genetic testing has, therefore, become commonplace for rare disease patients. Through current approaches, however, we only find a genetic diagnosis in around half of all rare disease patients. These approaches almost exclusively focus on the regions of the genome that code directly for proteins.

We believe that a subset of the undiagnosed patients will have genetic variants in regions outside of this protein-coding sequence, that have crucial roles in regulating the amount and location of proteins that are produced (by regulating transcript, translation, or cellular localisation). Our research uses large genomic datasets (including UK Biobank and the Genomics England 100,000 Genomes Project) and computational approaches to identify these disease-causing regulatory variants and determine how they lead to disease. By identifying these variants, we hope to influence clinical genetic testing guidelines and allow a valuable genetic diagnosis to be returned to more rare disease patients. We also create tools and resources to enable the results of our research to be used to help patients in the clinic.

We are also interested more generally in the role of variants in untranslated regions (UTRs) in common as well as rare disease, and how they influence penetrance and disease severity. To study this, we integrate large-scale multi-omics data (from e.g. the UK Biobank) including ribosome profiling and proteomics datasets.

Projects will be 100% bioinformatics based and tailored to individual interests. Please get in touch if you are interested in joining the team.

Project areas: Bioinformatics, Genomics, Translational regulation, Rare Disease, Clinical Genetics

*These pages were reviewed/updated:* ***26th September 2022***

*Our team*

We are a small team of currently seven individuals. We are an inclusive and supportive group with a strong focus on kindness, collaboration and mentorship.

*Key recent papers*

1. Ellingford JM, Ahn JW, Bagnall RD, … and Whiffin N. Recommendations for clinical interpretation of variants found in non-coding regions of the genome. **Genome Medicine** 2022: <https://doi.org/10.1186/s13073-022-01073-3>
2. Wright CF, Quaife NM, Ramos-Hernández L, … and Whiffin N. Non-coding variants upstream of MEF2C cause severe developmental disorder through three distinct loss-of-function mechanisms. **AJHG** 2021: https://doi.org/10.1016/j.ajhg.2021.04.025
3. Zhang X, Theotokis PI, Li N, ..., Whiffin N\* and Ware JS\*. Genetic constraint at single amino acid resolution improves missense variant prioritisation and gene discovery. **medRxiv** 2022: <https://doi.org/10.1101/2022.02.16.22271023>
4. Zhang X, Wakeling M, Ware JS and Whiffin N. Annotating high-impact 5’untranslated region variants with the UTRannotator. **Bioinformatics** btaa783 2021: <https://doi.org/10.1093/bioinformatics/btaa783>
5. Whiffin N, Karczewski KJ, Zhang X et al. Characterising the loss-of-function impact of 5' untranslated region variants in whole genome sequence data from 15,708 individuals. **Nature Communications** 2020: <https://doi.org/10.1038/s41467-019-10717-9>