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CHRONOGRAPHY OF INFLAMMATORY BOWEL DISEASE

# Year 2001: Link between susceptibility to Crohn's disease and variations in LRR☆

## Año 2001: asociación entre la susceptibilidad a la enfermedad de Crohn y las variaciones de LRR

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It was already known that Crohn's disease has a crucial genetic aetiological component due to its very different concordance in monozygotic twins (37%) compared to that in dizygotic twins (7%). In 1996, Jean-Pierre Hugot et al. published the first genome-wide association study identifying a locus of susceptibility to Crohn's disease adjacent to the centromere of chromosome 16, called *IBD1*. In 2001 two articles were published in the same issue of the journal *Nature* (one of which we analyzed in detail in the next infographic) which described the gene and the various polymorphisms of *IBD1* that confer susceptibility to the disease. Inherited susceptibility to Crohn's disease associated with NOD2 gene polymorphisms behave in part as an inherited genetic metering effect and in part as a recessive autosomal inheritance. Thus, heterozygotes have a slight increase in risk (relative risk of 3), while compound heterozygotes and homozygotes have a high relative risk (relative risk of 44 and 38, respectively). We also wished to single out from these two papers the work done by Hugot's group, since Professor Miquel Àngel Gassull was one of the first authors in said study, to our great appreciation. In recent years, a multitude of papers have continued to be published related to both Crohn's disease and ulcerative colitis and the various genes and polymorphisms thereof (more than 240 risk *loci)*. However, the genetic component is still only able to explain a small percentage (less than 30%) of the overall effect of susceptibility to IBD, which suggests a need to deepen the study of environmental factors and intestinal microbiota as crucial elements for the onset and perpetuation of the disease.

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## Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease

Hugot J-P, Chamaillard M, Zouali H, Lesage S, Cézard J-P, Belaiches J, et al. Nature. 2001;411:599-603

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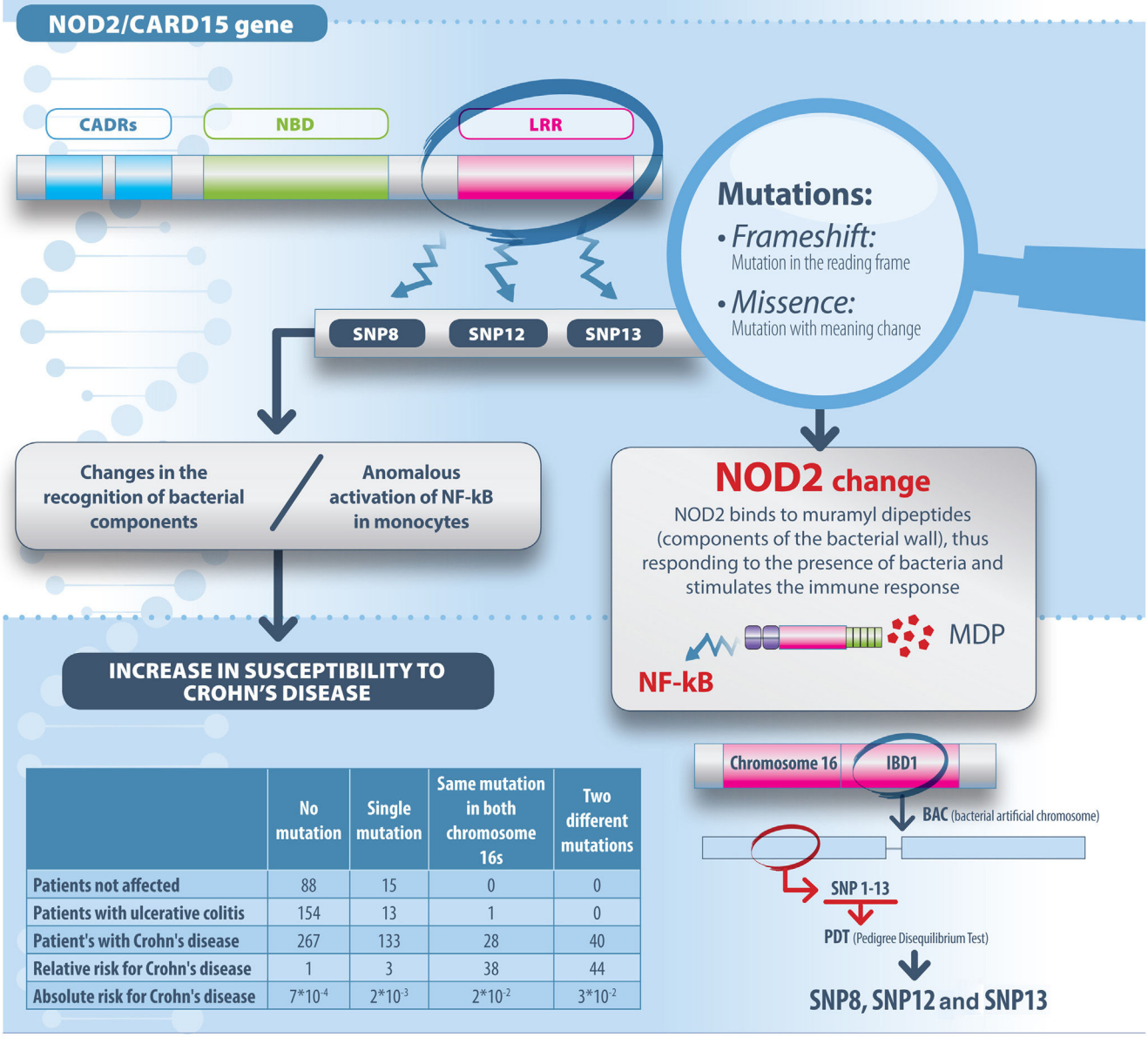
### Introduction

A locus of susceptibility to Crohn's disease is mapped in chromosome 16, using a strategy of positional cloning, based on an analysis of links followed by a mapping of linkage disequilibrium to identify a frameshift mutation and two missense mutations.




| | No mutation | Single mutation | Same mutation in both chromosome 16s | Two different mutations |
|---|---|---|---|---|
| Patients not affected | 88 | 15 | 0 | 0 |
| Patients with ulcerative colitis | 154 | 13 | 1 | 0 |
| Patient's with Crohn's disease | 267 | 133 | 28 | 40 |
| Relative risk for Crohn's disease | 1 | 3 | 38 | 44 |
| Absolute risk for Crohn's disease | $7*10^{-4}$ | $2*10^{-3}$ | $2*10^{-2}$ | $3*10^{-2}$ |