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## Mutations in genes required for pathogen defenses as a basis for breast cancer

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In-depth functional analyses of thousands of breast cancer gene mutations reveal different sets of mutated genes in hundreds of different breast cancer genomes. Despite differences in which genes are mutated, innate immunity pathways, signals to adaptive immunity, metabolic reactions supporting immune responses and structural barriers to infection are always abnormal. Many of these mutations have predictable associations with some kind of infection, including all known tumor viruses. Mutations may be rare individually but each set of mutations affects the ability to recognize pathogens and to defend against them. Infections and mutations can both contribute to cancer because they deregulate the same pathways. The frequency of an individual mutation may be less important than its effect on function. This work demonstrates that acquired immune deficiencies and immune dysregulation in cancer can occur because of mutations. Differences in immune responses caused by mutation represent a hidden variable in breast cancer-viral association studies. Compensating for these abnormalities may open many new opportunities for cancer prevention and therapy.

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