Smoke signals for lung disease

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Emphysema is a lung disease that is predicted to become one of the top five causes of death and disability worldwide by 2020. Cigarette smoking is the greatest risk factor for this disease. Despite this correlation, however, only about 15–20% of cigarette smokers develop emphysema. The fact that these susceptible individuals are generally clustered into families hints that there may be certain genes that predispose people to smoking-induced emphysema.

Unlike asthma, in which the flow of air through the lungs is temporarily obstructed, emphysema is characterized by a progressive airflow restriction that results in permanent enlargement of the lungs’ peripheral air spaces and loss of lung elasticity. In smoking-related emphysema these changes are often attributed to the destruction of lung connective tissue through enzymatic degradation of elastin, the main component of the elastic fibres of lung tissue.

Matrix metalloproteinases (MMPs) are zinc-dependent enzymes that can degrade connective tissues, including elastic fibres. The gene for the MMP12 protein in particular has been considered a strong candidate for conferring susceptibility to emphysema. MMP12 is produced by macrophages — inflammatory cells that infiltrate smokers’ lungs — and destroys not only elastin itself, but also elastin precursors.