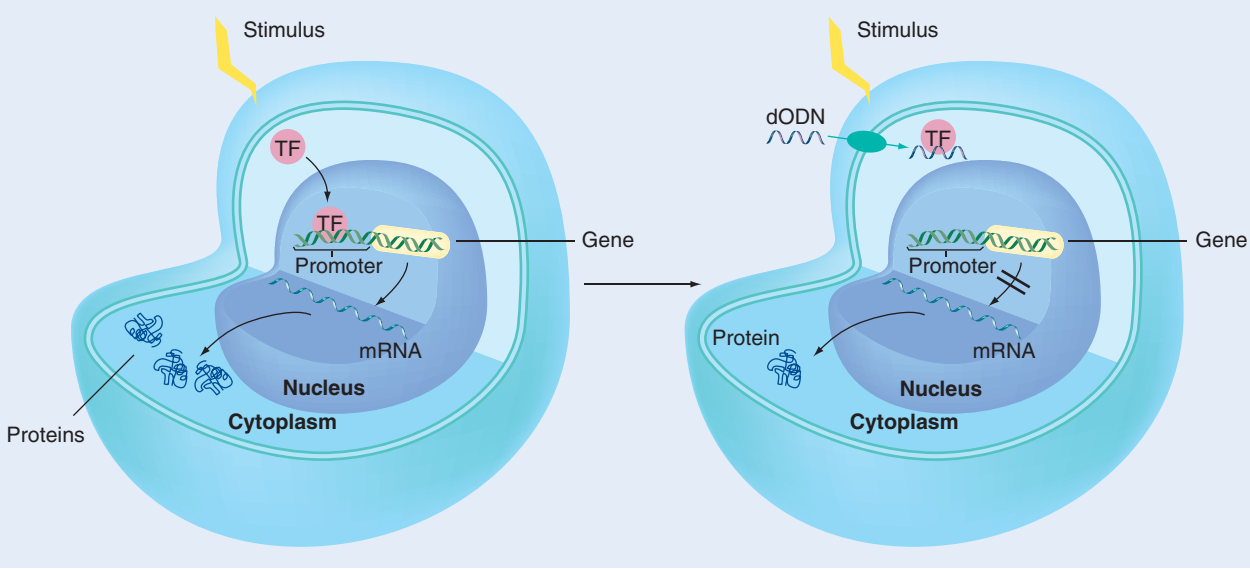
**Figure 1. The gene-silencing action of dODN.**




dODN: Decoy oligonucleotides; TF: Transcription factor.
Adapted with permission from Markus Hecker.

there are no limiting factors for their formulation and development as aerosols, droplets, ointments or injectables.

Rapid expansion of our understanding of the diversity of transcription factors and the roles that these regulatory proteins play in normal and abnormal cellular function has demonstrated the design, investigation and development of transcription factor decoy technology as appealing. Papers published on the ability to use decoys as research tools or as potential therapies continue to grow each year and a few examples of models in which decoys have been studied include inflammation, ranging from arthritis and sepsis (nuclear factor [NF]κB), to allergic airway reactivity and asthma (signal transducer and activator of transcription [STAT] 1 and NFkB), to glomerulonephritis (E2F and AP1) [5]. A large number of decoy applications in cancer have also been investigated, including colorectal and ovarian cancer (CRE), melanoma (SP1) and breast cancer (CRE, estrogen receptor and NFkB).

One of the best-studied applications of decoys to date is targeted to inhibit NFκB [5]. In particular, this target is attractive since it has been reported to act as a 'master switch', not only in response to proinflammatory stimulation to drive a cellular response, but also towards intra- and extra-cellular processes. Numerous stimuli are known to transactivate NFκB, including oxidative stress, ultraviolet radiation, proinflammatory cytokines, such as interleukin-1 and tumor necrosis factor-α, and lipopolysaccharide. Thus, strategies and agents to inhibit NFκB may present attractive therapeutic targets that have greater specificity compared with other anti-inflammatory drugs, such as the corticosteroid family of drugs.

The most advanced clinical program involving the use of transcription factor decoys reported to date involves the modification of the biology of bypass vein-graft failure via intraoperative delivery of decoys that inhibit postoperative neointimal hyperplasia. In this case, decoys specifically targeting NFκB, C/EBP and AP1 have all been studied [5,6]. Other clinical trials are also underway and initiated to examine specifically the STAT1 decoy on reactive airway disease and NFκB on atopic dermatitis.

## Future perspective

During the next 5 years, we should start to observe an increase in the number of clinical trials involving treatment with decoys around the globe, in its movement from bench to bedside. Despite the fact that decoys are seemingly proving to have positive effects in ongoing clinical trials, an important point to consider is that hundreds of transcription factors have been described and grouped, primarily by the consensus DNA sequences to which they bind