A patients develop neutralizing antibodies against FVIII. In the case of interferon-β 1a (INF-β) used in the treatment of multiple sclerosis, approximately ca. 25% of the patients develop antibodies that neutralize the function of INF-β. On the other hand, treatment with the GLP-1 agonist exenatide derived from the Gila monster causes an antibody response in 30%–40% of the patients without any significant impact on the efficacy of the drug, although in some of the high antibody titer patients less efficacy was found indicating that the antibody response may have had an impact.

9.3.5.1 Predicting Immunogenicity

No reliable experimental methods for predicting immunogenicity currently exist, but some *in silico* predictions may provide useful information with respect to the consequences of mutations in the primary structure between analogs of relevance. As such, these methods could be of relevance in the *ranking* of otherwise equal protein analogs but are of no value for peptides with unnatural building blocks, conjugations to various molecular moieties, or other post-translational modifications since the models are based on the natural T-cell epitope repertoire. Ex vivo methods may be an alternative way to predict the level of T-cell stimulation. One method is to determine the T-cell response after incubation of representative pools of T cells from humans with the drug analogs and to then rank potential risk of similar drug candidates.

9.4 CONCLUDING REMARKS

Biopharmaceuticals will gain more market shares in various disease areas in the years to come. Predominantly, in the fields of inflammation, hemophilia, cancer, diabetes, inflammation, as well as infectious diseases, peptides and proteins have shown their value and huge potential. New methodologies for extending half-life will likely result in new analogs among peptides and proteins that possess even greater efficacy not only in existing fields but also in new types of diseases. Progress has also been made in the area of oral formulation of larger peptides and may offer new future opportunities within the oral delivery of peptide pharmaceuticals.

FURTHER READING

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