clearing of the bacteria from the bloodstream. CRP finds use in protecting against pneumococcal infections (93,94) *Salmonella enterica* (95) *Neisseria meningitidis* (96) and malaria parasite (97).

CRP, TLRs, and NOD proteins are all used for pattern-recognition signaling (98). CRP consists of five identical proteins that are arranged around a central pore (99). The CRP polypeptide has the following sequence (100,101).

```
1  mekllcflvl  tslshafgqt  dmsrkafvfp  kesdtsyvsl  kapltkplka  ftvclhfyte
61  lsstrgtvfs  rmpprdktmr  ffifwskdig  ysftvggsei  lfevpevtva  pvhictswes
121  asgivefwvd  gkprvrkslk  kgytvgaeas  iilgqeqdsf  ggnfegsqsl  vgdignvnmw
181 dfvlspdein  tiylggpfsp  nvlnwralky  evqgevftkp  qlwp
```

The biology of C-reactive protein is not well known, at least when compared to other aspects of immunology, such as the biology of T cells and antibodies. In fact, it has been said that, "[d]espite extensive studies spanning several decades, the exact role and mechanism of action of CRP as a modulator of inflammation has not been well defined" (102). For this reason, the available information is collected and outlined in this chapter. A knowledge of CRP's biology has direct relevance in persuading regulatory agencies to accept CRP as a biomarker in clinical trials.

Figure 18.5 outlines the pathway where interleukin-6 (IL-6) is expressed by leukocytes in an inflamed tissue, where the IL-6 travels through the bloodstream to the liver, and where the hepatocytes respond by expressing and secreting CRP. Injury to various parts of the body results in the expression of IL-6 as well as other cytokines, which dramatically stimulate hepatocytes to release CRP (103). This increase is part of an event called *acute phase response*.

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