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HPV vaccine: from vision to product

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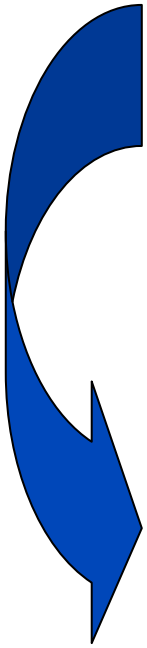
Infections as cause of human cancer

There is no straight proof for causality between infections and disease (cancer) in humans

- **epidemiologic profile of agent and disease**
- **biologic properties of the infectious agent**
- **experimental evidence (transformation of cells in culture, tumors in animals)**



- **vaccination**

Cervical cancer (CxCa): consequence of an infection

- Rigoni-Stern: report on cancer deaths in Verona (1842)
- early candidates: *T. palidum*, *N. gonorrheae*, HSV-2
- HSV-2: serologic evidence but no DNA in tumor samples
- HPV the rising star of the 1970s
  - malignant progression of PV-induced tumors in animals and in man
  - precursor lesions to CxCa (koilocytes) contain HPV particles

HPV and cervical cancer: pivotal discoveries

- 1977-80: heterogeneity of HPVs, genital HPVs
- 1983-84: HPV 16, 18
- 1984-89: consistent presence of HPV 16/18 DNA in CxCa
- 1986: presence of HPV 16/18 DNA favors progression of precursors
- since 1986: studies on mechanisms of viral transformation
- since 1987: other cancer-related HPV types
- 2008: Nobel Price to Harald zur Hausen

HPV vaccines: delay in development

- **Bosch and Munoz, 1988:**
  "Case-control studies conducted thus far were not planned as full epidemiological investigations and so none of them satisfies the usual criteria of design and analysis"
- **1980es: big pharma not interested**

HPV vaccines: finally the take-off

- **Munoz and Bosch, 1992:**

  "There is compelling evidence in favor of a causal interpretation of the association between HPV and cervical cancer".

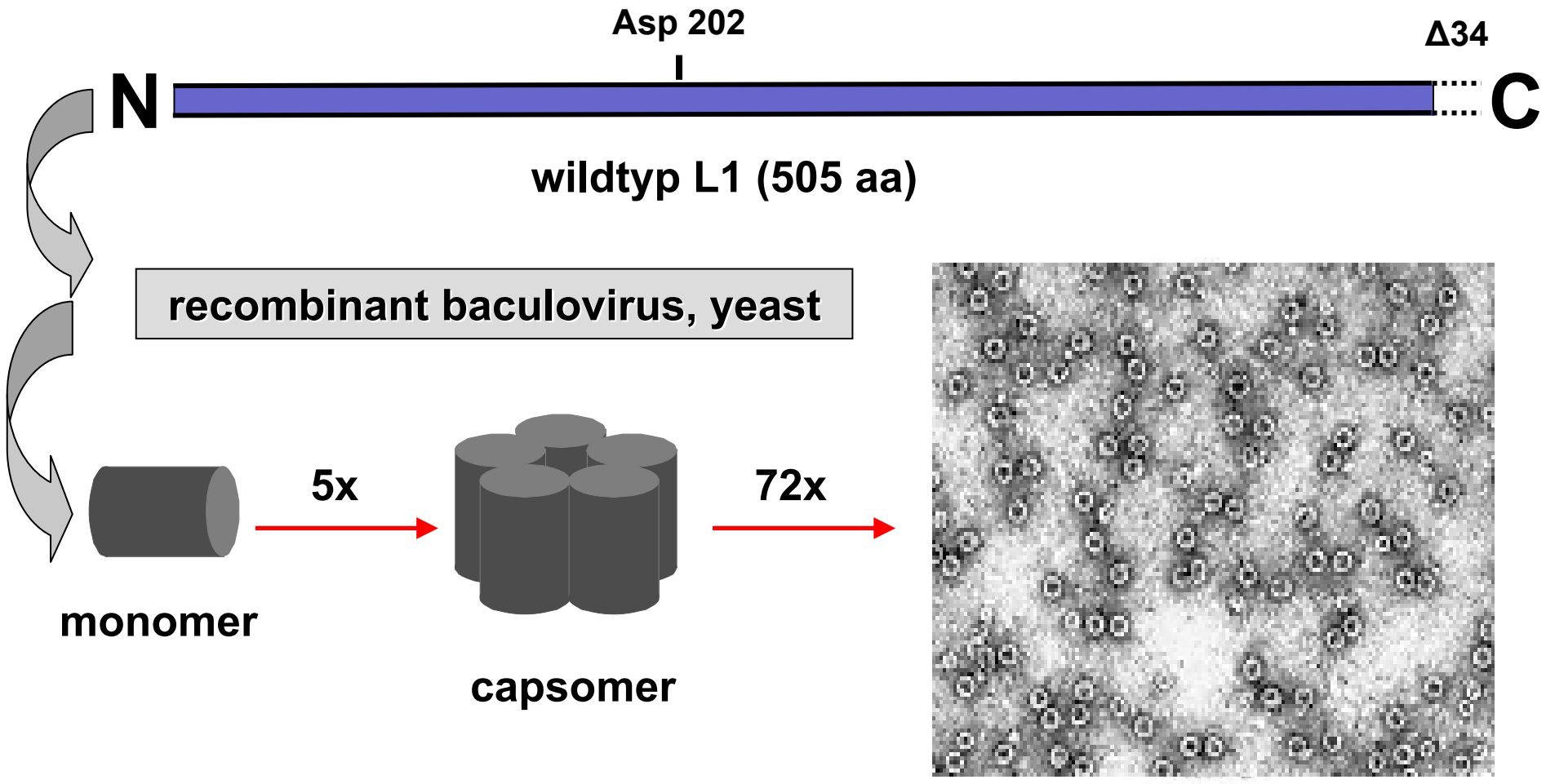
- **early 1990s: biotech start collecting IP and run first studies**
- **mid 1990s: technology transfer to Merck and GSK**
- **early 21nd century: first clinical trials**
- **2006: first launch (Gardasil)**
- **2008: 2nd product (Cervarix)**

HPV vaccines: synergism between academic and corporate activities

basic research: academia

- establishing the causal link
- establishing the mode of protection
- developing the concept of the vaccine

HPV vaccine (VLPs) consists of a single protein (L1)



Kirnbauer et al., J Virol 67:6929, 1993

HPV vaccines: synergism between academic and corporate activities

clinical development: companies

- manufacturing the vaccine
- testing safety in preclinical models
- establishing safety and immunogenicity
- establishing efficacy
- obtaining governmental approval

HPV vaccines are far from being perfect: 2nd generation

Shortcomings of the current vaccines

- Don‘t prevent all cases of CxCa
- are not therapeutic
- can‘t be used in copuntries of highest need

“The academic dilemma“

- Promising preclinical data with different vaccines
- Phase I trial required: 1-5 Mio EUR
- liaison with industry needed
- interest only with post-phase I data
- bridge funding is essential