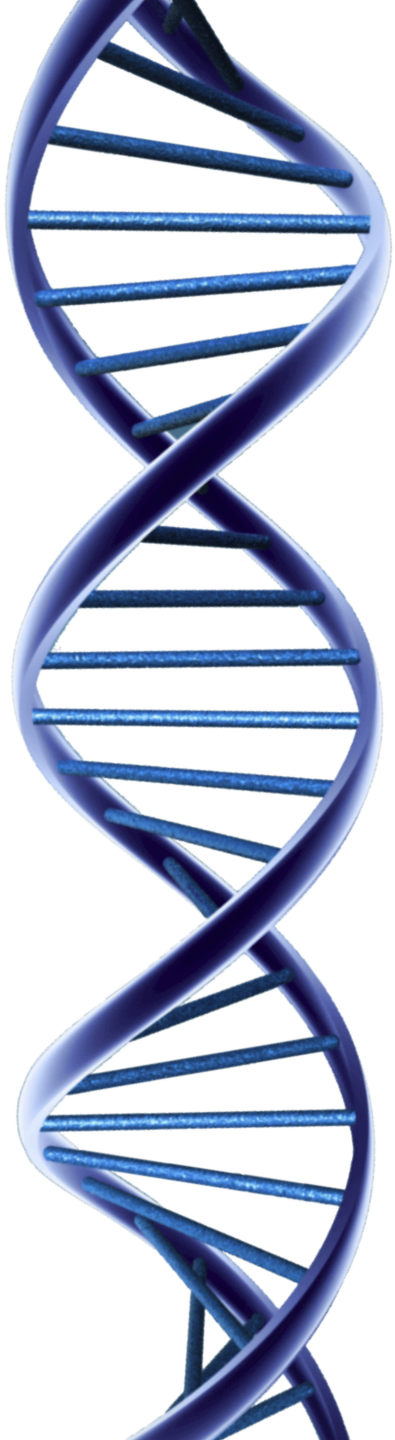

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New strategies, targets, and leads for male contraception

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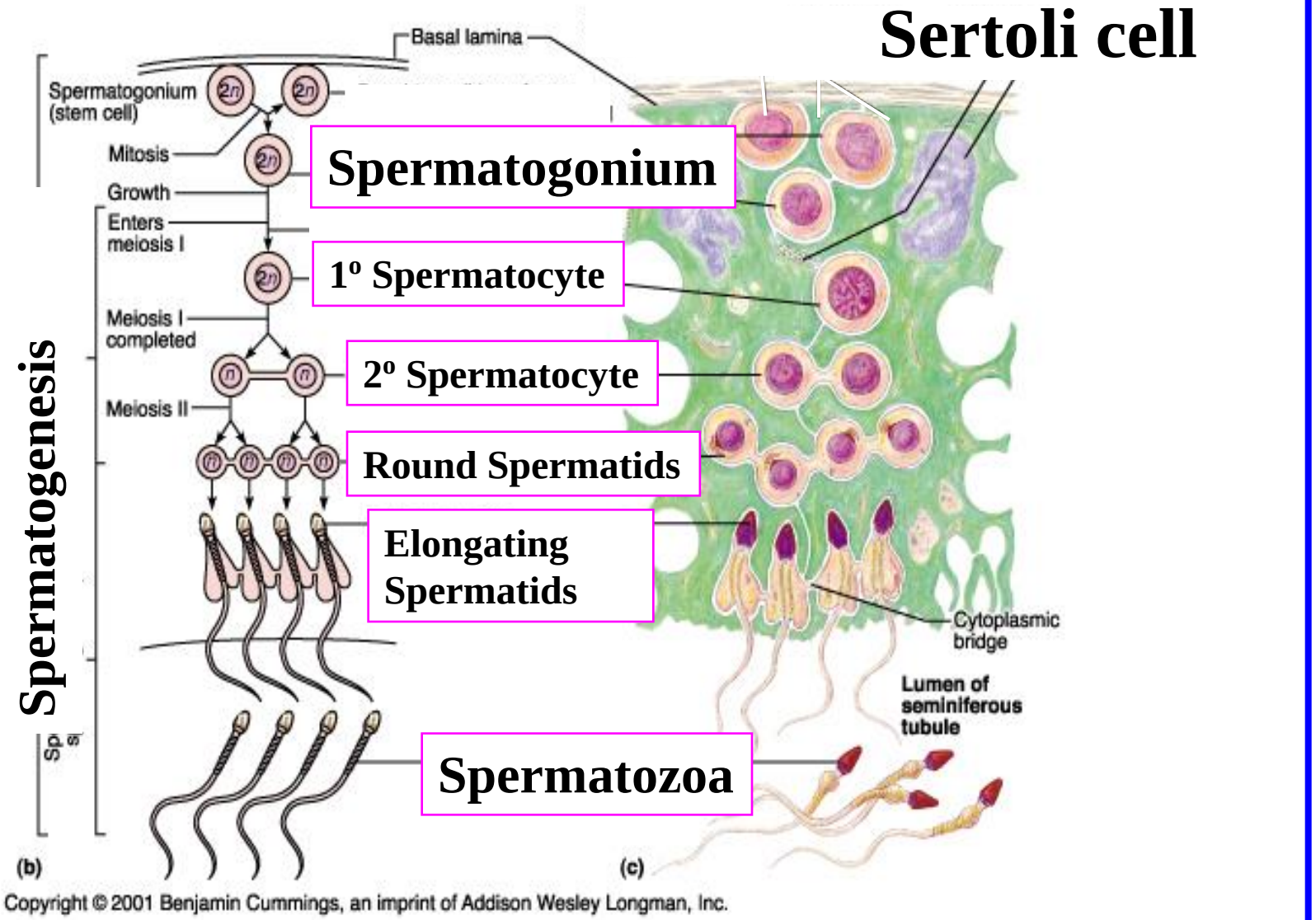
Paris, 5/6/16

Targeting male germ cells



- Constant proliferation of male germ cells, timeline of spermatogenesis, and blood-testis barrier present challenges to contraceptive development
- ~4% of mammalian genome expressed in (postmeiotic) male germ cells (Schultz, Hamra, and Garbers, *PNAS* 2003)
- Mutations in >1000 genes could cause infertility in men

Our approach to identify targets, chemical leads

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There are >1000 candidate infertility-associated genes, how does one:

- **Identify all of the "relevant" candidates?**
- **Uncover the best targets and discover acceptable small molecules to inhibit these candidates *at a reasonable cost*?**

Our approach:

Knock out candidate genes in mice to evaluate their roles in infertility and potential relevance to human contraception

Use a practical drug discovery and medicinal chemistry platform for identified targets: DNA-encoded chemical libraries, a cost effective and unique drug discovery tool.

A robust contraceptives pipeline is critical

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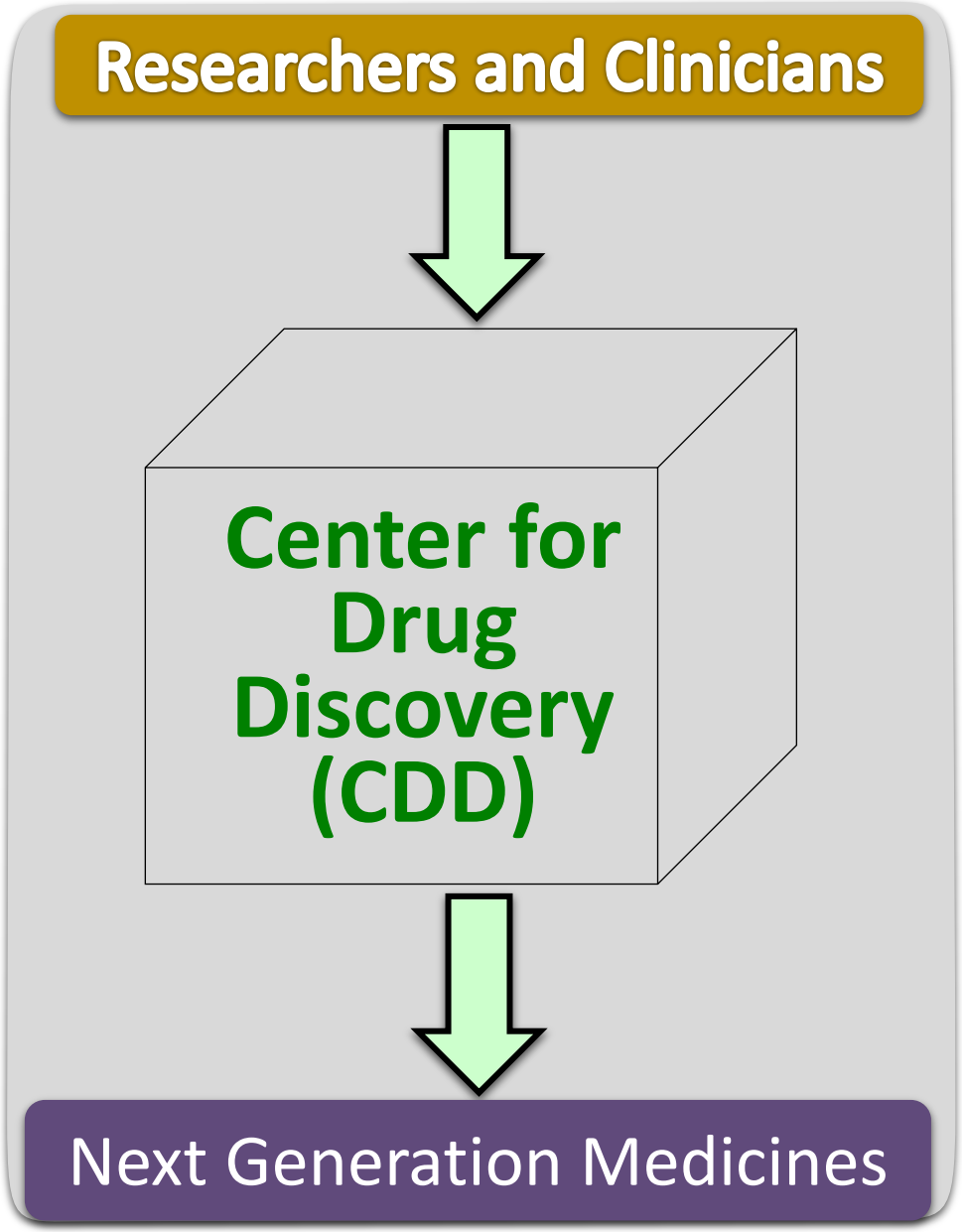

CDD Vision

To overcome both the high attrition rates of compounds entering preclinical development and the unique challenges of targeting male germ cells, it is critical to have a full pipeline of lead compounds.

The entry of dozens of phenotypically validated male contraception targets into an economical drug discovery platform will provide the quantity of leads necessary to ultimately produce a **non-hormonal** small-molecule male contraceptive.