Approach	Advantages	Disadvantages
Computational searches for TCF binding sites Position-weight matrices constructed based on validated lists of TCF binding sites can be used to screen *cis*-regulatory DNA for additional sites (e.g. 109). The efficiency of this approach can be improved by adding multiple sequences bound by TFs (e.g. helper sites in invertebrates; see 69). The functional relevance of binding sites can be verified with reporter assays.	• Quickly identifies potentially regulated genes • The identification of binding sites also establishes candidates for mutagenesis to rigorously test their functionality	• Most effective when the search space is restricted to short stretches of DNA (<20 kb) rather than the whole genome • Not all consensus TCF sites will be functional • TCFs and other TFs have degenerate binding sites that could be functional, which could be missed if the calling criteria are too stringent
Transcriptome analyses of Wnt-regulated genes Microarrays or RNA sequencing can be used to identify genes whose expression changes in Wnt-on and Wnt-off conditions in cell culture (e.g. 74) or embryos (e.g. 30)	• Identifies the full array of genes regulated by Wnt pathway activation • Many genetic and biochemical reagents are available to manipulate the Wnt pathway	• Does not distinguish between direct and indirect targets of Wnt signaling • *In vivo* analyses in animal tissues are limited by the specificity of the genetic drivers used for the manipulations
Chromatin immunoprecipitation sequencing (ChIP-seq) analyses of TCF or β-catenin genomic occupancy ChIP-seq with TCFs and β-catenin with or without Wnt activation can identify candidate Wnt-regulated enhancers. This approach can be combined with ChIP-seq for other TFs (e.g. 76) or with transcriptome analyses to assign genes to regulatory DNA sequences (e.g. 30).	• Biochemically establishes the presence of Wnt effectors at cis-regulatory elements • Provides evidence of direct regulation by the Wnt pathway	• Many TCF/β-catenin binding sites have no detectable function • Quality of the antibody used plays a major role • While this approach can identify putative Wnt-dependent cis-regulatory elements, identifying which gene the element regulates can be difficult, especially for long-range enhancers