Поиск тайных партнеров

Search for potential heterodimer complexes of bacterial transcription factors

Artemiy Bakulin, Anna Kaznadzey

Abstract

ExuR is a transcription factor of Escherichia coli believed to be a local regulator of hexuronate metabolism genes. Recent ChIP-Seq studies, partially performed at previous SMTB schools demonstrated that ExuR might regulate much more genes. Based on ChIP-Seq data, we have compiled a complete list of ExuR targets during growth on various media. ExuR may bind DNA directly or as a component of heteromeric complexes, e.g. with its homolog UxuR [Tutukina et al., 2016]. We have compared the ChIP-Seq-based list of targets with the results of SELEX experiment [shigen.nig.ac.jp] and divided the list into to parts: (i) genes directly regulated y UsuR and (ii) genes likely regulated by ExuR in complexes with other factors. We have estimated the frequency of heteromere regulatory interactions and listed candidate ExuR partners for each regulated gene. We have also predicted a candidate binding motif for ExuR.

ExuR — транскрипционный фактор Escherichia coli. Раньше он считался регулятором экспрессии генов гексуронатного метаболизма, однако в недавних исследованиях с применением метода ChiP-Seq, часть которых была проведена на предыдущих школах, было показано, что спектр мишеней ExuR должен быть значительно шире. Основываясь на результатах этих экспериментов, мы составили полный список мишеней ExuR при росте бактерий на разных средах.

Известно, что ExuR способен связываться как напрямую с ДНК, так и в составе гетеродимерных комплексов (например со своим гомологом UxuR [Tutukina et al, 2016]). Сопоставление с данными SELEX [shigen.nig.ac.jp] позволило нам разделить полученный список на (а) гены, работу которых ExuR регулирует, непосредственно связываясь с ДНК, и (б) гены, регуляция которых происходит при связывании ExuR с другими транскрипционными факторами. Мы выяснили, насколько часто происходит образование гетеродимеров, а также составили список потенциальных партнеров ExuR для найденных мишеней. Кроме того, был предсказан новый мотив связывания ExuR.

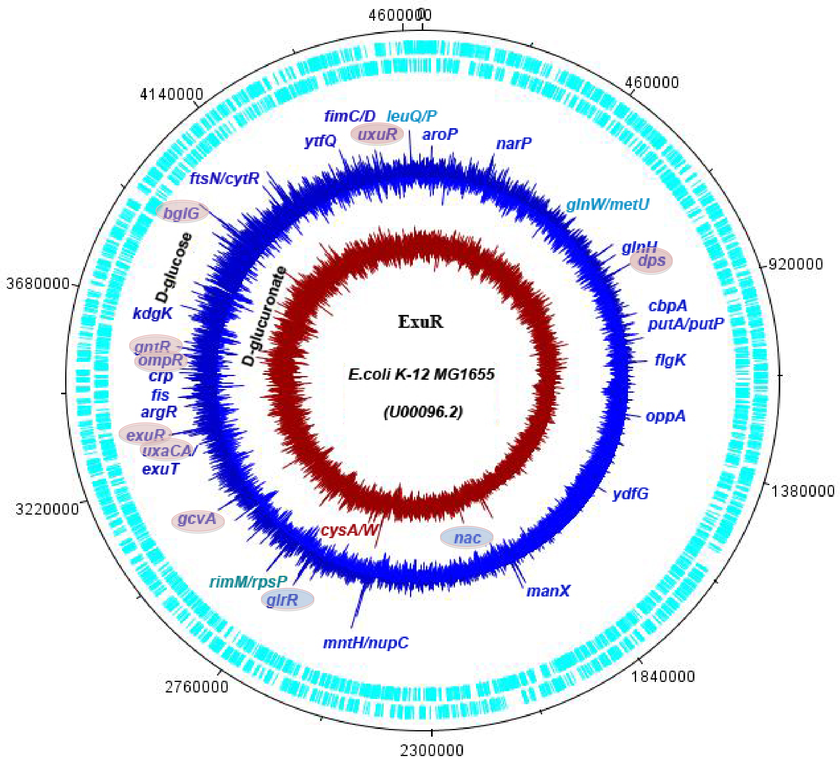

Figure3. ChIP-Seq peaks mapped on *E. coli* genome

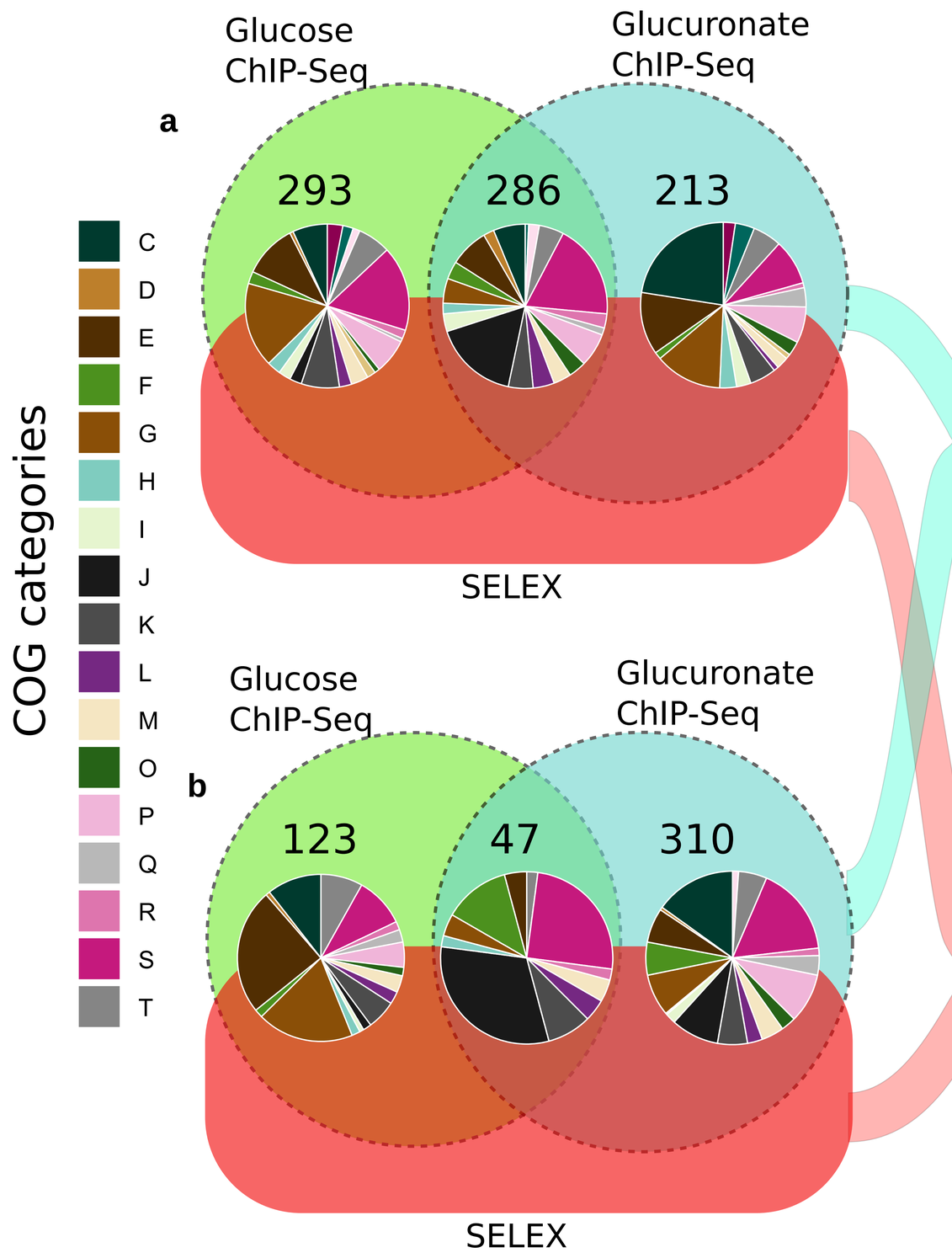

Figure 1. The distribution of target genes by function
a, b represent the same idea with different ChIP-Seq replicas
The inner diagrams show the distribution of genes by their COG categories

Sugar	Gene	Operon	SELEX	UxuR	Predicted regulators (RegulonDB)	Metabolic class	Function (GenBank)
Gln	aceA	aceBAK	S+	U+	IclR, CRP, Cra, IHF, ArcA	C	isocitrate lyase
Gln	aceE	pdhR-aceEF-lpd	S+	U+	PdhR, CRP, Cra, FNR	C	pyruvate dehydrogenase (decarboxylase component)
Gln	aceF	pdhR-aceEF-lpd	S+	U+	PdhR, CRP, Cra, FNR	C	pyruvate dehydrogenase (dihydrolipoyltransacetylase component)
Gln	aceK	aceBAK	S+	U+	IclR, CRP, Cra, IHF, ArcA	T	isocitrate dehydrogenase kinase/phosphatase
Gln	acnB	acnB	S+	U+	Fis, CRP, Cra, ArcA	C	aconitate hydrase B
Gln	acs	acs-yjcH-actP	S+	U+	Fis, CRP, IHF	I	acetyl-CoA synthetase
Gln	agaC	agaS-kbaY-agaBCDI	S+	U-	AgaR		PTS system N-acetylgalactosamine-specific IIC component 1

Table 1. Some genes that are regulated by ExuR

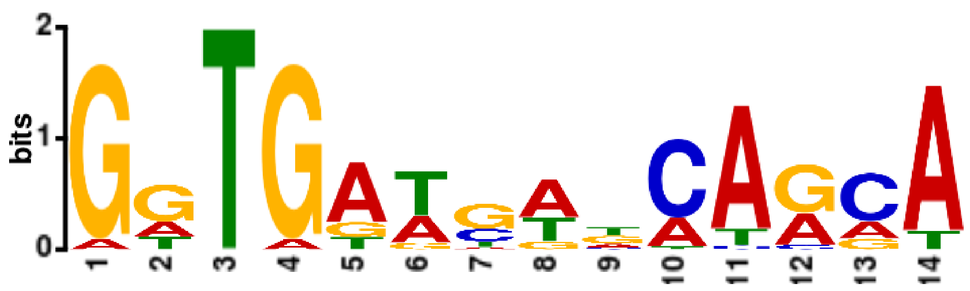

Figure 2. ExuR binding motif

Methods

ChIP-Seq and SELEX are experimental techniques used to analyze protein-DNA interactions. ChIP-Seq output consists of DNA sequences to which a protein binds either directly or in a complex with another transcription factor, while SELEX identifies sites to which a protein binds directly. We have compared the data of ChIP-Seq derived from bacteria cultured at different mediums (glucose, glucuronate) and deduced which genes are regulated by ExuR. Then we compared these genes with SELEX data.

At the intersection of ChIP-Seq and SELEX datasets we have found genes which are regulated by ExuR directly. Then we have applied motif discovery tools (ChiPMunk and MEME) to find shared motifs in ChIP-Seq peaks. We have discovered the list of genes which are regulated through this motif.

For genes identified in ChIP-Seq experiments but not in SELEX we searched for other regulators that could be potential partners of ExuR in heterodimeric complexes.

Results

We have identified the motif to which ExuR binds directly

We found 29 genes that are regulated through this motif:
ptsG, yciU, manY, tyrP, uvrY, asnU, cbl, fruK, napC, glpB, yfbV, fabB, yagI, metZ, metW, yhhA, ugpQ, uspA, yhjG, glnA, argB, argI, glnK, seqA, cydA, moaA, glnH, yliE, artP.

We have compiled the list of genes which are controlled by ExuR in heterodimers. Among those are genes involved in translation, ribosomal structure and biogenesis (J), genes of unknown functions (S) and genes involved in amino acid transport and metabolism (E). Their regulators could be partners of ExuR.

Лаборатория сравнительной и функциональной геномики
Laboratory of comparative and functional genomics